EPA Registration File
9402-10
Vol 1- Part 1

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

December 12, 2004

MEMORANDUM:

Efficacy Review EPA Reg. No. 9402-10 *Kleenex Anti-Viral Tissue*
DP Barcode 311439

From: Nancy Whyte, Efficacy Team Leader (Acting)
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

To: Adam Heyward, PM Team 34
Regulatory Management Branch II
Antimicrobials Division (7510C)

Thru: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Applicant:: Kimberly-Clark Corporation
2100 Winchester Road
Neenah, Wisconsin 54956

Formulation Label: **% by wt.**

Active Ingredient(s)

Citric acid	7.53%
Sodium lauryl sulfate	2.02%
Other ingredients	90.49%
Total	100.0%

I. Background:

The report of efficacy data conducted by Hill Top Research, Inc., Cincinnati, OH to determine the effectiveness of the product against Rhinovirus 2, ATCC VR-482 was received by the Product Science Branch on December 10, 2004. The testing had been done in February 2003 and was reported in MRID No. 4568754-01. Testing previously done against this organism in 2002 was not acceptable to support a label claim for effectiveness of the product

against Rhinovirus 2 because the recoverable virus titer achieved in the testing was not 10^4 for any of the three product lots tested. Efficacy data submitted at that time for four other organisms, Rhinovirus 1, ATCC VR-1364, Influenzae A, ATCC,VR-1469, Influenzae virus B, CDC !D# 2001701156 and Respiratory Syncytial Virus, ATCC VR-26 had been accepted in support of label claims. The testing was done using Good Laboratory Practices, and a Quality Assurance Statement was included in the testing report to the Agency.

II. Use Directions:

The use directions printed on the package label state that the product is to be used as a facial tissue, and has not been tested against bacteria, fungi, or other viruses. The tissues are to stored in a dry area, and disposed of promptly after use.

III. Agency Standards for Proposed Claims:

The effectiveness of virucides against specific viruses must be supported by efficacy data that simulates, to the extent possible in the laboratory, the conditions under which the product is intended to be used. Carrier methods that are modifications of either the AOAC Use-Dilution Method (for liquid disinfectants) or the AOAC Germicidal Spray Products Test (for spray disinfectants) must be used in developing data for virucides intended for use upon dry inanimate, environmental surfaces (e.g., floors, tables, cleaned dried medical instruments). To simulate in-use conditions, the specific virus to be treated must be inoculated onto hard surfaces, allowed to dry, and then treated with the product according to the directions for use on the product label. One surface for each of two different batches of disinfectant must be tested against a recoverable virus titer of at least 10^4 from the test surface for a specified exposure period at room temperature. Then, the virus must be assayed by an appropriate virological technique with multiple replicates per dilution. The calculated viral titers must be reported with the test results. For the data to be considered acceptable, results must demonstrate complete inactivation of the virus at all dilutions. When cytotoxicity is evident, at least a 3-log reduction in titer must be demonstrated beyond the cytotoxic level. These Agency standards are presented in DIS/TSS-7.

IV. Summary of Study:

There were no specific details presented about the actual testing procedure or the preparation of the virus prior to testing. A Protocol to Measure the Virucidal Efficacy of Facial Tissues prepared by Hilltop Laboratories was included in the testing report. This document outlined the experimental design for such testing, and contained a copy of Efficacy Data Requirements for Virucides proposed by the Registration Division, Office of Pesticide Programs of the Agency in 1976 which are consistent with the requirements of DIS/TSS-7 (see above). Results of the testing were reported as follows on the next page of this review.

Inoculating Facial Tissue Disks at 15 Minute Exposure Period against Rhinovirus 2, ATCC VR-482

Log_{10} $TCID_{50}$/0.1 mL*

Test Substance	Average Titer**	Reduction in Virus Titer	Percent Reduction in Virus Titer
3-7-02-4A	0.5*	4.3	>99.99
3-7-02-4B	0.5	4.3	>99.99
3-7-02-4C 60 da. stability sample	0.5	4.3	>99.99
3-7-02-4D Control	NA	NA	NA

* Triplicate runs
NA= Not Applicable

Results of Virucidal Tests Rhinovirus 2, ATCC VR-482

Sample: 3-7-02-4A
Control: 3-7-02-4D

CYTOPATHIC EFFECT						
Dilution Inoculated	Virus Control*			Sample + Virus*		
	a	b	c	a	b	c
10^{-1}	++++	++++	++++	0000	0000	0000
10^{-2}	++++	++++	++++	0000	0000	0000
10^{-3}	++++	++++	++++	0000	0000	0000
10^{-4}	++++	++++	+00+	0000	0000	0000
10^{-5}	0++0	0+0+	000+	0000	0000	0000
10^{-6}	0000	0000	0000	0000	0000	0000
Viral Titer (Log_{10}**$TCID_{50}$/0.1 mL)	5.0	5.2	4.2	0.5	0.5	0.5
Average Viral Titer (Log_{10}**$TCID_{50}$/0.1 mL)	4.8			0.5		

*Triplicate runs
Note: + = virus recovered: 0 = no virus recovered
$TCID_{50}$ Calculated by method of Reed and Muench

Results of Virucidal Test for Rhinovirus 2, ATCC VR-482

Sample: 3-7-02-4B
Control 3-7-02-4D

CYTOPATHIC EFFECT						
Dilution Inoculated	**Virus Control***			**Sample + Virus***		
	a	**b**	**c**	**a**	**b**	**c**
10^{-1}	++++	++++	++++	0000	0000	0000
10^{-2}	++++	++++	++++	0000	0000	0000
10^{-3}	++++	++++	++++	0000	0000	0000
10^{-4}	++++	++++	+00+	0000	0000	0000
10^{-5}	0++0	0+0+	000+	0000	0000	0000
10^{-6}	0000	000+	0000	0000	0000	0000
Viral Titer (Log_{10}**$TCID_{50}$/0.1 mL)	5.0	5.2	4.2	0.5	0.5	0.5
Average Viral Titer (Log_{10}**$TCID_{50}$/0.1 mL)	4.8			0.5		

*Triplicate runs
Note: + = virus recovered: 0 = no virus recovered
$TCID_{50}$ Calculated by method of Reed and Muench

Results of Virucidal Test for Rhinovirus 2, ATCC VR-482

Sample: 3-7-02-4C (60 day Stability Study)
Control 3-7-02-4D

CYTOPATHIC EFFECT						
Dilution Inoculated	**Virus Control***			**Sample + Virus***		
	a	**b**	**c**	**a**	**b**	**c**
10^{-1}	++++	++++	++++	0000	0000	0000
10^{-2}	++++	++++	++++	0000	0000	0000
10^{-3}	++++	++++	++++	0000	0000	0000
10^{-4}	++++	++++	+00+	0000	0000	0000
10^{-5}	0++0	0+0+	000+	0000	0000	0000
10^{-6}	0000	000+	0000	0000	0000	0000
Viral Titer (Log_{10}**$TCID_{50}$/0.1 mL)	5.0	5.2	4.2	0.5	0.5	0.5
Average Viral Titer (Log_{10}**$TCID_{50}$/0.1 mL)	4.8			0.5		

*Triplicate runs
$TCID_{50}$ Calculated by method of Reed and Muench
Note: + = virus recovered: 0 = no virus recovered

VI. Recommendations and Comments

1. The original viral titer was at least 10^4 (average 4.8) and efficacy testing of the product, *Antiviral Kleenex Tissue,* achieved at least a 3 $\log_{10}$ reduction in virus titer as required by DIS/TSS-7.

2. The label claim, already appearing on the product packaging, that the product is effective against Rhinovirus 2, ATCC VR-482 following 15 minutes exposure to the product, is supported by the efficacy testing submitted to the Agency.

TASK ASSIGNMENT FORM
Antimicrobial Division/Regulatory Management Branch II

A	Completed by Product Manager		
PRODUCT REVIEWER: L McKelvin			RMB II TEAM 34
Description of Action: Labeling changes			EPA File Symbol/Reg No.: 9402-10
Decision No. 346071	Submission No. 257689		Fee for Service Action Code:
FQPA Action Code: 302	Non-FQPA Action Code:		Fee for Service Fee: $
	MONTH	DAY	YEAR
APPLICATION DATE	03	31	2004
EPA PIN DATE	04	02	2004
REVIEWER ASSIGNED DATE	04	05	2004
DATE DUE TO PM			2004
DATE DUE OUT OF AGENCY	07	01	2004

Type of Data:	Product Chemistry ☐	Acute Toxicology ☐	Efficacy ☐	Environmental Fate ☐	Ecological Effects ☐	Chronic Toxicology ☐	Exposure ☐

COMMENTS: *NOTE TO ARCTIC SLOPE - PLEASE COMPLETE PART B OF FORM.*

DP Barcode No(s):

B	For Arctic Slope Contract Only	
Contractor: Arctic Slope	Contract No.: 0332	ARCTIC SLOPE/MANAGER
Draft Task: Signature _____ _____ (Est. hrs)	Final Task: Signature _____ _____ (Total hrs)	
Reviewer's Comments: (1)		

Response Code: 17 Response Date: 5/25/04

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

May 25, 2004

Eliot I. Harrison
The Lewis & Harrison Consultants,
Agent for
Kimberly-Clark Corp.
122 C Street, NW Suite 740
Washington, DC 20001

Subject: **Kleenex® Brand Anti-Viral Tissue**
EPA Registration No. 9402-10
Application Dated March 31, 2004

Dear Mr. Harrison:

The labeling referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, is acceptable.

A stamped copy of the accepted labeling is enclosed for your records.

Should you have any questions or comments concerning this letter, please contact me at (703) 308-6422, or Lisa McKelvin at (703) 308-7496.

Sincerely,

Adam Heyward
Product Manager (34)
Regulatory Management Branch II
Antimicrobials Division (7510C)

Enlcosure

2

KILLS 99.9% OF COLD & FLU VIRUSES*

See bottom for use directions

Kleenex® Anti-Viral* BRAND TISSUE

120 3-PLY TISSUES 8.4 x 8.2 in / 21.3 x 20.8 cm

ACTIVE INGREDIENTS:	
Citric Acid	7.51%
Sodium Lauryl Sulfate	2.02%
INERT INGREDIENTS	90.47%
Total	100.00%

ACCEPTED

MAY 25 2004

Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide, registered under EPA Reg. No. 9402-10

(3)

Kleenex® BRAND TISSUE

New KLEENEX® Anti-Viral tissue kills 99.9% of Cold and Flu Viruses**

Because cold and flu viruses are often spread by hand contact, KLEENEX® Brand has developed a new tissue for your whole family. New! KLEENEX® Anti-Viral* tissue has three soft layers, including a moisture-activated middle layer that kills 99.9% of cold and flu viruses* in the tissue within 15 minutes. This product has not been tested against bacteria, fungi or other viruses. See below for anti-viral* details.

Kleenex® Anti-Viral BRAND TISSUE

LOOKING GLASS – BLUE

FPO

UPC

Directions for Use: It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Use only as a facial tissue.

***Virucidal Against:** Rhinoviruses Type 1A and 2 (Rhinoviruses are the leading cause of the common cold); Influenza A and Influenza B (causes of the flu); Respiratory Syncytial Virus (RSV–the leading cause of lower respiratory infection in children).

Storage and Disposal: Store in a dry area. Dispose of used tissues promptly. Do not reuse empty container.

1-800-553-3639 weekdays 8 a.m. to 4 p.m. CT

Distributed by Kimberly-Clark Global Sales, Inc.,
Dept. KAV-120, PO Box 2020, Neenah, WI 54957-2020
Printed in USA.
Made in the USA from domestic and imported material.

www.kleenex.com

120 3-PLY TISSUES 8.4 X 8.2 IN

This box is made from 100% recycled paper.

ACTIVE INGREDIENTS:

Citric Acid	7.51%
Sodium Lauryl Sulfate	2.02%
INERT INGREDIENTS	90.47%
Total	100.00%

EPA Reg. No.: 9402-10
EPA Est. No.: 009402-SC-002

Kleenex® BRAND TISSUE

Kleenex® BRAND TISSUE

(4)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

April 2, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

ELIOT I. HARRISON, AGENT FOR
KIMBERLY-CLARK CORP
122 C STREET, N.W. SUITE 740
WASHINGTON, D.C. 20001

PRODUCT NAME: KLEENEX BRAND ANTI-VIRAL TISSUE
COMPANY NAME: KIMBERLY-CLARK CORP
OPP IDENTIFICATION NUMBER: 297110
EPA FILE SYMBOL: 9402-10
EPA RECEIPT DATE: 04/02/04

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Antimicrobials Division, Risk Management Team 34, at (703) 308-6422.

Sincerely,

J Price

Front End Processing Staff
Information Services Branch
Information Resources and Services Division

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LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

March 31, 2004

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue**
EPA File Symbol No. 9402-10
Registrant: Kimberly-Clark Corporation
Minor Label Amendment

Dear Adam:

Inadvertently, there is a minor typographical error in the concentration of citric acid and the inert ingredients on the product label for Kleenex® Brand Anti-Viral Tissue. It appears that this error was made when the "printers proof" labels were developed.

The concentration of citric acid on the product label submitted with the original application and on the current Confidential Statement of Formula (CSF) is 7.51%. The concentration on the most current stamped label is 7.53%. The label concentration for citric acid should be 7.51%. In addition, the label concentration for the inert ingredients should be 90.47%, not 90.45%. Accordingly, I am submitting five (5) copies of a revised product label with the appropriate concentration of citric acid and the inert ingredients. A copy of the current CSF is also attached.

If you have any questions about this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot Harrison
Agent for Kimberly-Clark

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Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☐ Registration
☐ Amendment
☐ Other

OPP Identifier Number
297110

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification ☐ None ☐ Restricted
4. Company/Product (Name)	PM#	
5. Name and Address of Applicant *(Include ZIP Code)* ☐ *Check if this is a new address*	6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to: EPA Reg. No. _____ Product Name _____	

Section - II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) _____
*rtification must be submitted	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ Container		☐ On Label ☐ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title	
[signature]	Agent, Agt for Kimberly-Clark	(1)
4. Typed Name	5. Date	
	2/3/04	

Please read instructions on reverse before completing form. Form Approved, OMB No. 2070-0060, Approval expires 05-31-98

EPA United States Environmental Protection Agency Washington, DC 20460

☐ Registration ☒ Amendment ☐ Other

OPP Identifier Numbe: **297110**

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
9402-10	Adam Heyward	☒ None ☐ Restricte
4. Company/Product (Name)	PM#	
Kleenex® Brand Anti-Viral Tissue	Team 34	

5. Name and Address of Applicant *(Include ZIP Code)*
Kimberly-Clark
2100 Winchester Road
Neenah, WI 54956
☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:
EPA Reg. No.
Product Name

Section – II

☒ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated
☐ Notification – Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application
☐ Other - Explain below

Explanation: Use additional page(s) is necessary. (For Section I and Section II.)

Minor label amendment – correcting a typographical error on the product label's ingredient statement.
This action does not require a Registration Fee.

Section – III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging		Water Soluble Packaging		2. Type of Container
☐ Yes* ☐ No	☐ Yes ☐ No		☐ Yes ☐ No		☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☐ Other (Specifiy)
***Certification must be submitted**	If "Yes" Unit Packaging wgt.	No. per container	If "Yes" Package wgt.	No. per Container	

3. Location of Net Contents Information ☐ Label ☐ Container

4. Size(s) Retail Container

5. Location of Label Directions ☐ On Label ☐ On labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section – IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application)*

Name	Title	Telephone No. (Include Area Code)
Eliot I. Harrison	Agent for Kimberly-Clark Corp.	(202) 393-2903

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped) 8

2. Signature	3. Title
	Agent for Kimberly-Clark Corp.
4. Typed Name	5. Date
Eliot I. Harrison	March 31, 2004

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete White- EPA File Copy (original) Yellow- Applicant Cop

PM WORK ASSIGNMENT SHEET

DECISION 336075 PM 34

DESCRIPTION OF ACTION: r

SUBMISSION BAR CODE: S 750215

PRODUCT REVIEWER: Lisa

FILE SYMBOL/REG NO.: 9402-10

FQPA ACTION CODE: ~~700~~ ~~701~~ NON-FQPA ACTION CODE: 400

AMOUNT OF TIME TO COMPLETE TASK (ASRC only)	HOURS

	MONTH	DAY	YEAR
APPLICATION DATE	02	24	03
EPA PIN DATE	11	07	03
REVIEWER ASSIGNED DATE	11	12	03
DATE DUE OUT OF AGENCY			

TYPE OF DATA

Product Chemistry: ☐ Product Toxicology: ~~☒~~ Efficacy: ☐

RASSB: ☒ HED TOX ☐ ENVIRONMENTAL FATE ☐ FISH/WILDLIFE ☐

Other ☐

COMMENTS: MS. Vivian: Please Code out DP # (293383) with 37

JACKET(S)/FILE SHOULD BE SUBMITTED WITH YOUR LETTERS FOR SIGNATURE

RESPONSE CODE: 38 RESPONSE DATE: 5 / 12 / 04 (MO / Day / Year)

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MAR 10 2003

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

KIMBERLY-CLARK CORP
1400 HOLCOMB BRIDGE RD.
ROSWELL, GA 30076

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 03/03/03. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

(10)

458702-00

LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

February 26, 2003

Document Processing Desk - 6(a)(2)
Office of Pesticide Programs - 7504 (c)
U.S. Environmental Protection Agency
Crystal Mall #2
Arlington, VA 22202
attn: Adam Heyward, Product Manager (34)

re: Reportable Information Under FIFRA Section 6(a)(2)
Product: Kleenex® Brand Anti-Viral Tissue #2
EPA File Symbol No. 9402-RE
Active Ingredients: Citric Acid and Sodium Lauryl Sulfate

Dear Mr. Heyward:

On behalf of Kimberly-Clark Corporation, I am submitting pursuant to Section 6(a)(2) of FIFRA and EPA's regulations at 40 C.F.R. Part 159, a human clinical dermal study conducted with Kleenex® Brand Anti-Viral Tissue #2. A registration application for this product is currently pending with the Agency's Antimicrobial Division, Office of Pesticide Programs (AD/OPP). As discussed further below, Kimberly-Clark is confident that Kleenex® Brand Anti-Viral Tissue #2 is not a dermal irritant when used, as intended, as a facial tissue.

To support the registration of Kleenex® Brand Anti-Viral Tissue #2, Kimberly-Clark conducted a dermal irritation study in rabbits (OPPTS Guideline No. 870.2500). No irritation was observed in any of the test animals. Accordingly, Kleenex® Brand Anti-Viral Tissue #2 has been classified as non-irritating to skin. Separate from the dermal irritation study required by OPP for product registration, Kimberly-Clark, as do most other consumer product companies, conducted human clinical studies to evaluate whether Kleenex® Brand Anti-Viral Tissue #2 may cause either cumulative irritant contact dermatitis and/or allergic contact dermatitis. These human studies were performed under conditions that simulate both the intended use and potential significant misuse, of the Kleenex® Brand Anti-Viral Tissue #2.

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The allergic contact dermatitis study (titled, "Repeated Insult Patch Study", No. DS106902-2) clearly demonstrated that Kleenex® Brand Anti-Viral Tissue #2, irrespective of the patching conditions employed, did not cause allergic contact dermatitis.

The cumulative irritant contact dermatitis study (titled, "21-Consecutive-Day Cumulae Irritation Patch Study", No. DS310502-1) was performed under conditions that can b considered much more severe than the standard animal dermal irritation study. For example, in the human study the test material (Kleenex® Brand Anti-Viral Tissue #2) was applied to each study participant for 23.5 consecutive hours per day for 21 consecutive days. In the animal study, the test material was placed under a semi-occlusive patch for 4 hours. The four different human testing conditions were:

- Semi-occlusive patching of dry tissue (simulates intended use);
- Semi-occlusive patching of wet tissue (simulates misuse);
- Occlusive patching of dry tissue (simulates significant misuse); and
- Occlusive patching of wet tissue (simulates significant misuse).

It is important to emphasize that occlusive patching was employed in order to evaluate potential significant product misuse, such as feminine hygiene use as a temporary tampon substitute or temporary occluded pad substitute.

Under conditions that simulated the intended use of Kleenex® Brand Anti-Viral Tissue #2 (semi-occlusive patch of dry test material/tissue), no irritation was observed in the study. Even under more severe test conditions (semi-occlusive patching of wet test material/tissue) the result was considered no different than the semi-occlusive patch with dry test material/tissue. Under conditions that simulated significant product misuse, moderate irritation was observed. However, even then, irritation was not seen until five days into the 21 day cumulative test. Thus, irritation would only occur if the misuse were both significant and continued for a longer period of time than could reasonably be expected for this product. Moreover, any irritation that did occur to the test participants during the study, dissipated after use of the test material/tissue was discontinued, and there was no permanent damage to the underlying dermis.

Based on the results of the human studies, Kimberly-Clark is confident that Kleenex® Brand Anti-Viral Tissue #2, is not a dermal irritant when used as intended, as a facial tissue. Consistent with EPA packaging/labeling requirements, the package label will clearly indicate "For use only as a facial tissue".

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If you have questions about this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

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LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

February 26, 2003

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RE
Applicant: Kimberly-Clark Corporation
Registration Application for New Product
Data Transmittal Letter for Studies being Submitted in Response to Your Correspondence of November 25, 2002

Dear Adam:

On behalf of Kimberly-Clark Corporation, I am submitting the following studies pursuant to FIFRA 6(a)(2):

- Volume 1 of 2
  21-Consecutive-Day Cumulative Irritation Patch Study
  MRID# 45870201

- Volume 2 of 2
  Repeated Insult Patch Study
  MRID# 45870202

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

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MEMORANDUM

Date: September 30, 2003

Subject: **6 (a)(2) Screening for Kleenex® Brand Anti-Viral Tissue #2**

EPA Reg: 9402-10
Kleenex® Brand Anti-Viral Tissue #2
DP Barcodes: D293383
PC Code:021801, Citric Acid

From: Deborah Smegal, Toxicologist,
Risk Assessment and Science Support Branch (RASSB), Antimicrobials Division (AD)[7510C]

To: Adam Heyward, PM 34
Sharon Carlisle, PM Team Reviewer
Regulatory Management Branch
Antimicrobials Division [7510C]

Thru: Norman Cook, Chief, RASSB/AD [7510C]

Applicant: Kimberly-Clark Corp, Roswell, GA.

Synonym: None

ACTION REQUESTED: Re: "21-Consecutive-Day Cumulative Irritation Patch Study" and "Repeated Insult Patch Study". Review the attached submission for 6 (a)(2) screening, MRIDs 458702-01 and 458702-02. .

CONCLUSIONS: This study is a human clinical study which is not usually reviewed by this Agency. However, the material shows cumulative moderate irritation in humans under occlusive conditions that simulate product misuse, but no irritation under semi-occlusive patching, which simulates intended use. There was no evidence of sensitization. RASSB concludes this substance, as noted in the above studies, does not require an expedited review.

Note: Hard copy of the study and administrative information will be returned to Norm Cook.

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November 7, 2003

NOTE TO PM 34: Adam Heyward

The following data package(s) have been screened for 6(a)2 and do not require expedited review:

Registration Number	MRID	6(a)2 Data Package Number
9402-10	458702-01 and 457802-02	DP# 293383
1529-40	45919200	DP# 293386

All data, administrative materials and science reviewers comments are attached for your review if provided. I consider this issue resolved and no further action is necessary by the 6(a)2 coordinator at this time.

Thanks

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

May 12, 2004

Eliot I. Harrison
The Lewis & Harrison Consultants,
Agent for
Kimberly-Clark Corp.
122 C Street, NW, Suite 740
Washington, DC 20001

Subject: **Kleenex ® Brand Anti-Viral Tissue #2**
EPA Registration No. 9402-10
Letter Dated February 26, 2004
Receipt Date: March 3, 2003

Dear Mr. Harrison:

The following amendment, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, is acceptable.

Proposed Amendment

- Human clinical dermal study

General Comment

These studies are human clinical studies which are not usually reviewed by this Agency. However, the material shows cumulative moderate irritation in humans under occlusive conditions that simulate product misuse, but no irritation under semi-occlusive patching, which simulates intended use. There was no evidence of sensitization.

Should you have any questions or comments concerning this letter, please contact me at (703) 308-6422, or Lisa McKelvin at (703) 308-7496.

Sincerely,

Lisa McKelvin

Adam Heyward
Product Manager (34)
Regulatory Management Branch II
Antimicrobials Division (7510C)

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
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May 12, 2004

Eliot I. Harrison
The Lewis & Harrison Consultants,
Agent for
Kimberly-Clark Corp.
122 C Street, NW, Suite 740
Washington, DC 20001

Subject: **Kleenex ® Brand Anti-Viral Tissue #2**
EPA Registration No. 9402-10
Letter Dated February 26, 2004
Receipt Date: March 3, 2003

Dear Mr. Harrison:

The following amendment, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, is acceptable.

Proposed Amendment

- Human clinical dermal study

General Comment

These studies are human clinical studies which are not usually reviewed by this Agency. However, the material shows cumulative moderate irritation in humans under occlusive conditions that simulate product misuse, but no irritation under semi-occlusive patching, which simulates intended use. There was no evidence of sensitization.

Should you have any questions or comments concerning this letter, please contact me at (703) 308-6422, or Lisa McKelvin at (703) 308-7496.

Sincerely,

Lisa McKelvin for
Adam Heyward
Product Manager (34)
Regulatory Management Branch II
Antimicrobials Division (7510C)

18

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

May 12, 2004

Eliot I. Harrison
The Lewis & Harrison Consultants
Agent for
Kimberly-Clark Corp.
122 C Street, NW, Suite 740
Washington, DC 20001

FILE COPY

Subject: **Kleenex ® Brand Anti-Viral Tissue #2**
EPA Registration No. 9402-10
Letter Dated February 26, 2004
Receipt Date: March 3, 2003

Dear Mr. Harrison:

The following amendment, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, is acceptable.

Proposed Amendment

- Human clinical dermal study

General Comment

These studies are human clinical studies which are not usually reviewed by this Agency. However, the material shows cumulative moderate irritation in humans under occlusive conditions that simulate product misuse, but no irritation under semi-occlusive patching, which simulates intended use. There was no evidence of sensitization.

Should you have any questions or comments concerning this letter, please contact me at (703) 308-6422, or Lisa McKelvin at (703) 308-7496.

Sincerely,

Lisa McKelvin for

Adam Heyward
Product Manager (34)
Regulatory Management Branch II
Antimicrobials Division (7510C)

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Date: May 5, 2004

Subject: **Data Evaluation Reviews (DERs) for two human clinical studies with Kleenex® Brand Anti-Viral Tissue #2**

EPA Reg: 9402-10
Kleenex® Brand Anti-Viral Tissue #2
DP Barcodes: D296506
PC Code:021801, Citric Acid

From: Deborah Smegal, Toxicologist,
Risk Assessment and Science Support Branch (RASSB), Antimicrobials Division (AD)[7510C]

To: Adam Heyward, PM 34
Lisa McKelvin, PM Team Reviewer
Regulatory Management Branch
Antimicrobials Division [7510C]

Thru: Norman Cook, Chief, RASSB/AD [7510C]

Applicant: Kimberly-Clark Corp, Roswell, GA.

Synonym: None

ACTION REQUESTED: Re: "21-Consecutive-Day Cumulative Irritation Patch Study" and "Repeated Insult Patch Study". Review the attached human clinical studies (MRIDs 458702-01

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and 458702-02), and prepare Data evaluation Reviews (DERs)..

CONCLUSIONS: These studies are human clinical studies which are not usually reviewed by this Agency. However, the material shows cumulative moderate irritation in humans under occlusive conditions that simulate product misuse, but no irritation under semi-occlusive patching, which simulates intended use. There was no evidence of sensitization.

Note: Hard copy of the study and administrative information will be returned to Norm Cook.
Sign-off Date : 05/05/04
DP Barcode No. : D296506

TXR No. :

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EPA Primary Reviewer: Deborah Smegal, MPH
Risk Assessment and Science Support Branch,
Antimicrobials Division (7510C)
EPA Secondary Reviewer: Norm Cook
Risk Assessment and Science Support Branch,
Antimicrobials Division (7510C)

Signature: Deborah Smegal
Date May 5, 2004
Signature: Norm Cook
Date 5/7/04

TXR#:

DATA EVALUATION RECORD

STUDY TYPES: NON-GUIDELINE (Human Clinical Study for Skin Sensitization)

PC CODE: 021801

DP BARCODE: 296506
SUBMISSION NO.: not provided

TEST MATERIAL (PURITY): Identification number is 2416.05. Description is white tissue with blue dots. No other statements about the active ingredient in the test material or its purity were provided. **Letter from Registrant (2/26/2003) identifies active ingredient as citric acid.**

SYNONYMS: not provided

CITATION: Dosik, J.S. 2002. Repeated Insult Patch Study (2002). TKL Study No. DS106902-2. KC Study No. 2416 (2416.05). MRID 458702-02

SPONSOR: Kimberly-Clark Corporation (Neenah, Wisconsin)

EXECUTIVE SUMMARY:

In a primary dermal sensitization study (MRID 458702-02) test material 2416.05 having an unknown active ingredient, human test participants were tested using a repeated insult patch study. A total of 197, mostly Caucasian female subjects completed the study. The name of the method used for this test was not specified. The study consisted of nine inductions with the test material and three challenge phases (e.g., challenge phases performed over 48 hour, 72 hour, and 96 hour time periods). The patch was applied to the subjects back, either to the right or left of the midline, or to the upper arm. The material was affixed to the skin using an occlusive patch. The skin sites were scored during the nine induction periods, a make up period, and during the three challenge phases.

The nine induction readings indicate that primarily erythema with no edema increased over time for all the subjects. This maximum elicited response occurred in 45.5% of the subjects completing induction. Damage to the epidermis exhibited by oozing, crusting and/or superficial erosions also occurred. However, this effect was the maximum elicited response in only 6.0% of the patients. There was a significantly lower response in the 48 hour challenge phase (3/197 or 1.5% with edema and no damage to epidermis) and an even lower response for the 72 hour challenge phase (1/197 or 0.5% with edema and no damage to epidermis). This study indicates

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the test material may be an irritant. **The study indicates the test material (2416.05) is not a dermal sensitizer.**

This study is classified as **Unacceptable/Non-guideline** (upgradable) because of the following deficiencies:

1) Lack of information regarding the active ingredient in the test material and purity.
2) The study was **not** conducted in accordance with EPA Good Laboratory Practices (GLPs).
3) The name of the test method used for this study was not specified.
4) No protocol documentation of the test method was provided.
5) The study did not provide a positive control to compare results.

COMPLIANCE: A written statement was provided which indicated that the study was not conducted in accordance with EPA Good Laboratory Practice (GLP) standards, as specified in 40 CFR Part 160 and that no information in this study is being claimed confidential on the basis of its falling within the scope of FIFRA Section 10 (d)(1)(A), (B), or (C). This report is a clinical research study performed by TKL in accordance with all applicable federal regulations and proposed guidelines for Good Clinical Practices, which include: Investigational New Drug Application (21 CFR Part 312), Protection of Human Subjects (21 CFR Part 50), and Institutional Review Boards (21 CFR Part 56).

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:	Test Code No. 2416.05 (No statements about active ingredient and purity %) A letter from the registrant (2/26/03) accompanying the study submission identifies citric acid as the active ingredient.
Description:	white tissue with blue dots 8-27-02A (two 1 lb bags)
Lot/Batch #:	not provided
Purity:	not provided
CAS # of TGAI:	not provided

2. Vehicle and/or positive control:

There was no vehicle control used for TKL Study No. DS106902-2. No positive controls were used for this study.

3. Study Population:

Age at start:	18 years or older

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Medical history: All subjects were required to complete medical history and consent forms and meet all study requirements (not specified). Females of child bearing potential were required to practice accepted forms of birth control. Volunteers were excluded from the study for the following reasons:

- had any visible skin disease at the study site which, in the opinion of the investigative personnel, would have interfered with the evaluation;
- were receiving systemic or topical drugs or medication which, in the opinion of the investigative personnel, would have interfered with the study results;
- had psoriasis and/or active atopic dermatitis/eczema;
- were females who were pregnant, planning to become pregnant during the study, or breast-feeding; and/or
- had a known sensitivity to cosmetics, skin care products, or topical drugs as related to the material being evaluated.

B. STUDY DESIGN and METHODS:

1. Test dates:

TKL Study # DS106902-2. KC Study No. 2416 (2416.05).
Start: 09/11/2002 End: 10/31/2002

2. Subject assignment and treatment:

The "Repeated Insult Patch study" [TKL Study # DS106902-2, KC Study No. 2416 (2416.05)] followed a protocol approved on September 5, 2002. The protocol outlining the specific treatment procedures for conducting this study was not provided in the study report. However, the study report did provide an overview of study procedures. A description of the study is as follows.

Subjects participated in the study over a 6-week period involving 3 phases: (1) Induction, (2) Rest, and (3) Challenge. Prior to study entry, the subjects were screened to assure that they met the inclusion/exclusion criteria. Informed consent was obtained. Each subject was provided with a schedule of the study activities and all subjects were told to avoid wetting patches and asked not to engage in activities that caused excessive perspiration. They were instructed to notify the staff if they experienced any discomfort beyond mild itching or observed any adverse changes at the patch sites, during the study or within 2 weeks of completing the study.

Of the 209 subjects enrolled, 197 mostly Caucasian female subjects completed the study.

The Induction Phase consisted of 9 consecutive applications of the study material and subsequent evaluations of the patch sites. Prior to application of the patches, the sites were outlined with a skin marker, e.g., gentian violet. The subjects were required to remove the patches approximately 24 hours after application. They returned to the facility at 48-hour intervals to have the sites evaluated and identical patches applied to the same sites. Patches applied on Friday were removed by the subjects after 24 hours. The sites were evaluated on the following Monday, i.e., 72 hours after patch application.

Following the ninth evaluation, the subjects were dismissed for a rest period of

approximately 10-15 days.

Subjects who were absent once during the induction phase received a make-up (MU) patch at the last induction visit. The MU applications were graded 48 hours later at the MU visit, or were recorded as N9G (no ninth graded).

The Challenge Phase was initiated during the sixth week of the study. Identical patches were applied to sites previously unexposed to the study material. The patches were removed by subjects after 24 hours and the sites graded after additional 24-hour and 48-hour periods (i.e., 48 and 72 hours after application). Rechallenge was performed whenever there was evidence of possible sensitization.

To be considered a completed case, a subject must have had 9 applications and no fewer than 8 subsequent readings during induction, and a single application and 2 readings during challenge. Only completed cases were used to assess sensitization.

The patch was applied to the intrascapular area of the subjects back, either to the right or left of the midline, or to the upper arm. Material evaluated under occlusive patch conditions was applied to a 2-cm x 2-cm Webril pad attached to a non-porous, plastic film adhesive bandage (3M medical tape). The patch was secured with hypoallergenic tape (Micropore).

3. Definitions used for Grading Response:

The skin site was scored using the following scale:

- = no reaction;
? = minimal or doubtful response, slightly different from surrounding normal skin;
+ = definite erythema, no edema;
++ = definite erythema, definite edema;
+++ = definite erythema, definite edema and vesiculation.

Special notations:

E= marked/severe erythema,
S= spreading of reaction beyond patch site,
p= papular response >50%,
pv = papulovesicular response >50%,
D = damage to epidermis: oozing, crusting and/or superficial erosions,
I= itching,
X = subject absent,
PD= patch dislodged,
NA = not applied,
NP = not patched, and
N9G= no ninth grading.

(25)

II. RESULTS:

A. INDUCTION READINGS:

The induction readings indicate that primarily erythema with no edema increased over time for all the subjects. This effect was the maximum elicited response in 45.5% of the subjects completing induction. Damage to the epidermis exhibited by oozing, crusting and/or superficial erosions also occurred. However, this effect was the maximum elicited response in only 6.0% of the patients. Table 1 is a reproduction of the data presented in the study (see page 21 of 48 in the study report). Definitions of skin scores were provided in the study design and method section. Table 2 is a summary of this data (see page 21 of 48 in the study report).

B. CHALLENGE PHASE:

Based on the lower response difference of the 48 hr challenge phase (1.5% with edema and no damage to epidermis) and even lower response of the 72 hr challenge phase (0.5% with edema and no damage to epidermis) in Table 1 to the higher responses characterized in the induction phase, the authors were correct in concluding that the results did not indicate sensitization after multiple inductions.

TABLE 1. Summary of Dermatologic Response Grades
Number of Subjects

Response	Induction Reading										Challenge Phase		
	1	2	3	4	5	6	7	8	9	Make-up	48 hr	72 hr	96 hr
'-'	191	165	137	112	87	77	63	55	58	11	167	174	
'?'	11	31	52	57	65	68	65	58	50	2	27	22	1
'?!'	0	0	0	0	0	0	0	0	1	0	0	0	
'+'	0	4	10	24	40	55	71	81	87	11	3	1	
'+I'	0	0	0	0	1	0	1	1	1	0	0	0	
'+D'	0	0	0	3	3	1	1	4	0	0	0	0	
Total	202	200	199	196	196	201	201	199	197	24	197	197	1

- = no reaction; ? = minimal or doubtful response, slightly different from surrounding normal skin; + = definite erythema, no edema; I= itching; D = damage to epidermis: oozing, crusting and/or superficial erosions

TABLE 2. Maximum Elicited Response During Induction*

Response	n (%) Subjects
'-'	40 (20.0%)
'?'	54 (27.0%)
'?I'	1 (0.5%)
'+'	91 (45.5%)
'+I'	2 (1.0%)
'+D'	12 (6.0%)

*All subjects completing induction (n=200)

C. POSITIVE CONTROL: No positive controls were used in any of the studies.

III. DISCUSSION

A. INVESTIGATOR'S CONCLUSIONS: Under the conditions employed in the study, there was no evidence of sensitization to Test Code No. 2416.05.

B. REVIEWER'S DISCUSSION/CONCLUSIONS:
The investigator's conclusions seem appropriate from the results. However, the actual active ingredients or concentrations were not reported. Several other deficiencies with the study are noted below.

C. DEFICIENCIES: The study was classified as **Unacceptable/Non-guideline** for the following deficiencies:
1) Complete lack of information regarding the active ingredient and purity of the test material.
2) The study was **not** conducted in accordance with EPA Good Laboratory Practices (GLPs).
3) The type of test method was not specified.
4) FDA recommends testing a minimum of 200 subjects to demonstrate a negative skin sensitization response (http://www.fda.gov/cdrh/ode/944.html) . In this study the actual number of subjects is 197.
5) No protocol documentation was provided.
6) The study did not provide a positive control to compare results.

D. STUDY CLASSIFICATION: This study is classified as **Unacceptable/Non-guideline** (upgradable) because of the deficiencies noted above.

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EPA Primary Reviewer: Deborah Smegal, MPH **Signature:** Deborah Smegal
Risk Assessment and Science Support Branch,
Antimicrobials Division (7510C) **Date** May 5, 2004
EPA Secondary Reviewer: Norm Cook **Signature:** Norm Cook
Risk Assessment and Science Support Branch,
Antimicrobials Division (7510C) **Date** 5/7/04

TXR#:

DATA EVALUATION RECORD

STUDY TYPES: NON-GUIDELINE (Human Clinical Study for Cumulative Skin Irritation)

PC CODE: 021801

DP BARCODE: 296506
SUBMISSION NO.: not provided

TEST MATERIAL (PURITY): Unknown (Not Reported) **Letter from Registrant (2/26/2003) identifies active ingredient as citric acid.**

SYNONYMS: not provided

CITATION: Dosik, JS. (2003) IAL). 21-Consecutive-Day Cumulative Irritation Patch Study. TKL Study #DS310502-1, KC Study # 2425A. MRID 458702-01. Unpublished.

SPONSOR: Kimberly-Clark Corporation (Neenah, WI)

EXECUTIVE SUMMARY: A dermal irritation study (MRID 458702-01) with human participants was conducted with six test materials having an unknown active ingredient in tissue paper. The concentration or purity of the active ingredient was also not reported. In the study, the test material was applied to the skin using a 21-consecutive-day cumulative irritation patch study to determine their ability to cause irritation to the skin of normal volunteer subjects. J&J baby oil served as a negative control. Sodium lauryl sulfate, 0.2% w/v aqueous solution, served as a positive control. Twenty-four, mostly Caucasian female subjects, completed the study, who were between the ages of 32 and 73 years of age. However, only 18 subjects completed the test with 2425.02, while 22 subjects completed the test with 2425.07 due to skin damage resulting from these compounds.

The study consisted of 21-consecutive day application with the test material. In each case, the patch was applied to the subjects back, either to the right or left of the midline, or to the upper arm. The material was affixed to the skin using either an occlusive patch or a semi-occlusive patch. Twenty-four hours later the patches were removed, the sites evaluated, the responses recorded, and identical patches applied to the same sites. The skin site was scored each day for each subject participating in the study.

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Four of the six test materials exhibited no significant irritation. Two test materials, 2425.02 and 2425.07, both patched occlusively, were moderately irritating, and resulted in skin damage to 12 and 8 subjects, respectively.

This study is classified as **Unacceptable/Non-guideline** (upgradable) because of the following deficiencies:

- Purity, concentration, and stability of the test material in bulk, as well as the homogeneity, concentration, and stability of the test article in distilled water were not provided;
- The study was **not** conducted in accordance with EPA Good Laboratory Practices (GLPs) as specified in 40 CFR Part 160.
- The Protocol specifies that 30 subjects should be tested and only 24 made it through the completion of the study.
- No protocol documentation was provided.

COMPLIANCE: No information in this study is being claimed confidential on the basis of its falling within the scope of FIFRA Section 10 (d)(1)(A),(B), or (C). A signed and dated statement indicated that this study was not conducted in accordance with EPA Good Laboratory Practice (GLP) standards, as specified in 40 C.F.R. Part 160. A signed statement of quality assurance was provided documenting that the report has been reviewed by the TKL Research, Inc. (TKL) Corporate Assurance Department and that the report accurately reflects the raw data for this study. The report also documents that the study was performed in accordance with all applicable federal regulations and proposed guidelines for Good Clinical Practices which include 21 CFR Part 312 (Investigational New Drug Application), 21 CFR Part 150 (Protection of Human Subjects), and 21 CFR Part 56 (Institutional Review Boards).

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:	White Facial Tissue (possibly containing trace amounts of Sodium Lauryl Sulfate). Six study materials, Test Code #'s 2425.02, 2425.03, 2425.05, 2425.07*, 2425.08*, and 2425.10* (* = wet with 0.2 mL saline prior to patch application)
Description:	not provided
Lot/Batch #:	not provided
Purity:	not provided
CAS # of TGAI:	not provided

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No statement of purity, strength, and stability of the active ingredient was provided in the study report by the sponsor. Receipt of the substance was documented in a general logbook that serves as a permanent record of the receipt, storage, and disposition of all study material received by TKL Research, Inc.

2. **Vehicle and/or positive control**: The following vehicle controls were used: .

- Sodium Lauryl Sulfate, 0.2% w/v aqueous solution (positive control)
- J&J baby oil (negative control)

Sodium Lauryl Sulfate served as the positive control and J&J baby oil served as the negative control.

3. **Study Population**:

Age at start: 18 years or older

Medical history: Individuals were eligible for inclusion in the study if they:

- were males or females, 18 years of age or older, in general good health;
- were free of any systemic or dermatologic disorder which, in the opinion of the investigative personnel, would have interfered with the study results or increased the risk of adverse events;
- were of any skin type or race providing the skin pigmentation would allow discernment of erythema;
- had completed a patch evaluation Medical Screening form as well as a Medical/Personal History form; and
- had read, understood and signed an informed consent agreement.

Individuals were excluded from participation in the study if they:

- had any visible skin disease at the study site which, in the opinion of the investigative personnel, would have interfered with the evaluation;
- were receiving systemic or topical drugs or medication which, in the opinion of the investigative personnel, would have interfered with the study results;
- had psoriasis and/or active atopic dermatitis/eczema;
- were females who were pregnant, planning to become pregnant during the study, or breast-feeding; and/or
- had a known sensitivity to cosmetics, skin care products, or topical drugs as related to the material being evaluated.

B. STUDY DESIGN and METHODS:

1. Test dates:

The study was conducted from November 5, 2002 to November 27, 2002.

2. Subject assignment and treatment:

The procedure employed is a modification of a procedure described by Dr. B.M. Lanman[1] at the Joint Conference on Cosmetic Sciences, April 21-23, 1968 in Washington, D.C., and further modified by Phillips, et. al[2] and Berger, et. al[3]. Using these methods, for occlusive patch conditions, the study material and controls were applied to a 2-cm x 2-cm Webril pad attached to a non-porous, plastic film adhesive bandage (3M medical tape). The pad was affixed to the back skin with hypoallergenic tape (Micropore), as needed. For semi-occlusive patch conditions, the material was applied with a 2-cm x 2-cm Webril pad. The pad was affixed to the back skin with hypoallergenic tape (Micropore).

Each subject was exposed to all six test compounds, simultaneously. Subjects were between the ages of 32-73, and were mostly female (26 of 30 enrolled) and Caucasion (28 of 30 enrolled). A total of 24 subjects completed the study (21 females and 3 males).

The study extended over a 22-consecutive-day period with 21 product applications and evaluations. On Day 1, the study material and controls were applied to the back under conditions described in the previous paragraph. Twenty-four hours later the patches were removed, the sites evaluated, the responses recorded, and identical patches applied to the same sites. This was repeated daily for a total of 21 days including Saturdays and Sundays.

3. Definitions used for Grading Responses:

Responses were graded using the symbols listed in Table 1 below:

Table 1: Definitions Used for Grading Responses

Symbol	Response	Numerical Equivalent
-	no visible reaction	0

[1] B.M. Lanman, E.B. Elvers and C.J. Howard. "The Role of Human Patch Testing in a Product Development Program." Joint Conference on Cosmetic Sciences, The Toilet Goods Association, Washington, D.C., April 21-23, 1968.

[2] L.Philips, M. Steinberg, H.I. Maibach and W.A. Akers. "Comparison of Rabbit and Human Skin Response to Certain Irritants." Toxicol. Appl. Pharmacol. 21.369, 1972.

[3] R.S. Berger and J.P. Bowman. "A Reappraisal of the 21-day Cumulative Irritation Test in Man" J. Toxicol. - Cut. & Ocular Toxical. 1 (2). 109-115, 1982.

Symbol	Response	Numerical Equivalent
- with p, pv, d or combinations thereof	papular (p) or papulovesicular (pv) response and/or dryness (d) without erythema	0.5
?	Minimal/doubtful erythema (slightly different from surrounding normal skin)	1.0
? with p, pv, d or combinations thereof	Minimal/doubtful erythema accompanied by papular or papulovesicular response and/or dryness	1.5
+	Definite erythema	2.0
+ with p, pv, d, or combinations thereof	Definite erythema, accompanied by papular or papulovesicular response and/or dryness	2.5
++, +++	Definite erythema and definite edema (++) with vesicles (+++)	3.0
+D,++D,+++D	Definite erythema with or without severe damage to epidermis characterized by crusting, superficial erosions, or oozing (D)	3.0

The maximum obtainable individual score was 3.0. When a "++", "+++", "+D", "++D", or "+++D" reaction occurred at any point during the study, further patch evaluation on that subject was terminated. An irritation score for each product was calculated by summing each individual's scores on each of 21 consecutive days. The total score is the summation of scores for all individuals. The normalized score is the total score divided by the total number of the readings for all subjects and multiplied by 21 (the number of days) and by 10 (to normalize to 10 subjects).

II. RESULTS:

Using the methods reported in this study, 30 subjects enrolled in the study and 24 of the subjects completed all phases. Five subjects voluntarily discontinued the study, while one subject had a protocol violation. Fresh materials were applied 7 days per week for 21 days to the same site. Six study materials, were applied to each person simultaneously at different locations on the back. Test Code #'s 2425.02, 2425.03, 2425.07, and 2425.08 were applied occlusively, and 2425.05 and 2425.10 were applied semi-occlusively. The products were graded for irritation using the scale identified in Table 1. Table 2 provides the classification scale based on irritancy. This scale is normalized for 10 subjects.

Table 2: Irritancy Scores

Normalized Score	Classification
0-49	No significant irritation
50-199	Slightly irritating

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200-449	Moderately irritating
450-630	Highly irritating

The results of the occlusive and semi-occlusive readings for each test code number are shown on Table 3. A summary of dermal responses with skin irritation over time are presented in Table 4 and plotted for test materials with positive responses in Figures 1-3.

Table 3: Irritation Scores for the Test Materials

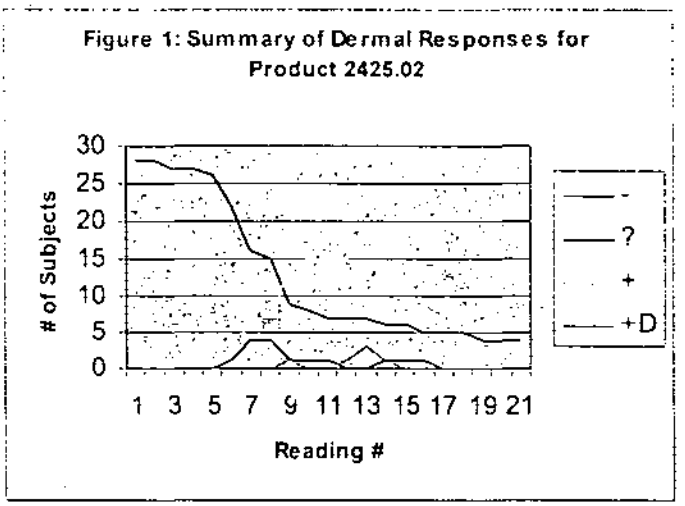
Test Code Number	Conditions	Number of Subjects Completing Test	Irritation Scores		Classification of Normalized Scores
			Total	Normalized	
2425.02	Occlusive	18	569.0	225.9	Moderately irritating
2425.03	Occlusive	24	0.0	0.0	No significant irritation
2425.05	Semi-occlusive	24	0.0	0.0	No significant irritation
2425.07	Occlusive	22	585.0	232.2	Moderately irritating
2425.08	Occlusive	24	0.0	0.0	No significant irritation
2425.10	Semi-Occlusive	24	18.0	7.1	No significant irritation
J&J baby oil (negative control)		24	0.0	0.0	No significant irritation
Sodium Lauryl Sulfate, 0.2% w/v aqueous solution (positive control)		0	1301.0	516.5	Highly irritating

Table 4: Summary of Dermatologic Response Grades
Number of Subjects by Product

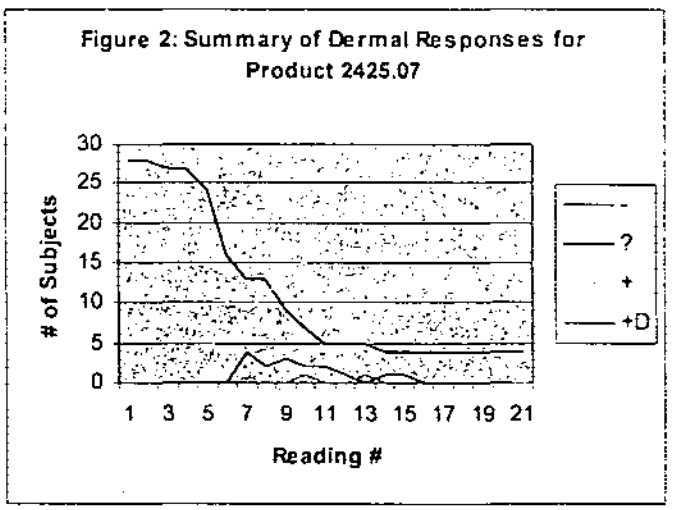
Product	2425.02 Fact Facial Tissue					2425.03 White Facial Tissue		2425.05 Fact Facial Tissue		2425.07 Fact Facial Tissue					2425.08 White Facial Tissue		2425.10 Fact Facial Tissue				J&J Baby Oil		SLS				
Reading #	-	?	+	+D	# Subjects Discontinued	-	# Subjects Discontinued	-	# Subjects Discontinued	-	?	+	+D	# Subjects Discontinued	-	# Subjects Discontinued	-	?	+	# Subjects Discontinued	-	# Subjects Discontinued	-	?	+	+D	# Subjects Discontinued
1	28	0	0	0	2	28	2	28	2	28	0	0	0	2	28	2	28	0	0	2	28	2	27	0	1	0	2
2	28	0	0	0	2	28	2	28	2	28	0	0	0	2	28	2	28	0	0	2	28	2	16	8	4	0	2
3	27	0	0	0	3	27	3	27	3	27	0	0	0	3	27	3	27	0	0	3	27	3	5	4	18	0	3
4	27	0	0	0	3	27	3	27	3	27	0	0	0	3	27	3	27	0	0	3	27	3	1	6	19	1	3
5	26	0	1	0	3	27	3	27	3	24	0	3	0	3	27	3	27	0	0	3	27	3	0	5	12	9	4
6	22	1	3	0	4	26	4	26	4	16	0	10	0	4	26	4	25	0	1	4	26	4	0	2	12	2	14
7	16	4	6	0	4	26	4	26	4	13	4	9	0	4	26	4	25	1	0	4	26	4	0	1	12	1	16
8	15	4	7	0	4	26	4	26	4	13	2	11	0	4	26	4	25	1	0	4	26	4	0	0	9	4	17
9	9	1	14	1	5	25	5	25	5	9	3	13	0	5	25	5	24	1	0	5	25	5	0	0	0	9	21
10	8	1	15	0	6	25	5	25	5	7	2	15	1	5	25	5	24	1	0	5	25	5	0	0	0	0	30
11	7	1	15	0	7	24	6	24	6	5	2	16	0	7	24	6	23	0	1	6	24	6	0	0	0	0	30
12	7	0	15	1	7	24	6	24	6	5	1	17	0	7	24	6	23	0	1	6	24	6	0	0	0	0	30
13	7	0	12	3	8	24	6	24	6	5	0	17	1	7	24	6	23	0	1	6	24	6	0	0	0	0	30
14	6	1	11	1	11	24	6	24	6	4	1	17	0	8	24	6	23	0	1	6	24	6	0	0	0	0	30
15	6	1	11	0	12	24	6	24	6	4	1	17	0	8	24	6	23	0	1	6	24	6	0	0	0	0	30
16	5	1	12	0	12	24	6	24	6	4	0	18	0	8	24	6	23	1	0	6	24	6	0	0	0	0	30
17	5	0	13	0	12	24	6	24	6	4	0	18	0	8	24	6	23	1	0	6	24	6	0	0	0	0	30
18	5	0	13	0	12	24	6	24	6	4	0	18	0	8	24	6	24	0	0	6	24	6	0	0	0	0	30
19	4	0	14	0	12	24	6	24	6	4	0	18	0	8	24	6	24	0	0	6	24	6	0	0	0	0	30
20	4	0	14	0	12	24	6	24	6	4	0	18	0	8	24	6	24	0	0	6	24	6	0	0	0	0	30
21	4	0	14	0	12	24	6	24	6	4	0	18	0	8	24	6	24	0	0	6	24	6	0	0	0	0	30

- = no reaction; ? = minimal or doubtful response; + = definite erythema, no edema; +D = damage to epidermis: oozing, crusting, and/or superficial erosions.

(34)

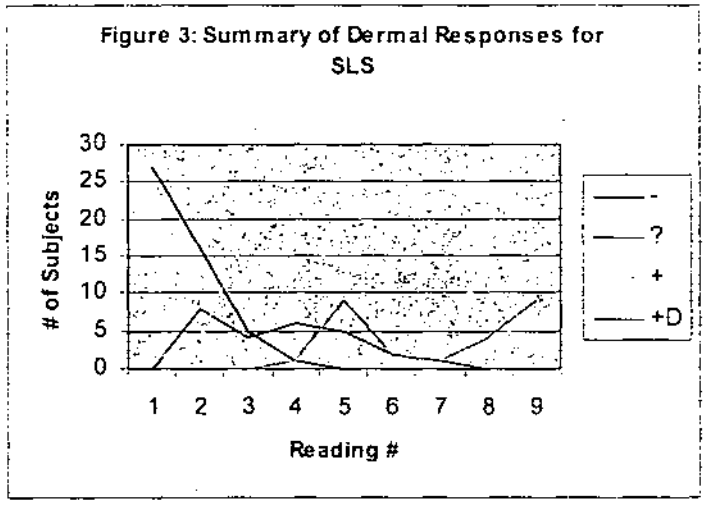


- No visible reaction
? Minimal/doubtful erythema
+ Definite erythema
+D Definite erythema with or without severe damage



- No visible reaction
? Minimal/doubtful erythema
+ Definite erythema
+D Definite erythema with or without severe damage

(5)



- No visible reaction
? Minimal/doubtful erythema
+ Definite erythema
+D Definite erythema with or without severe damage

From the results in Figures 1-3 it appears that at day 5 both products 2425.02 and 2425.07 induce erythema effects in some subjects and that at day 9, more subjects exhibit erythema then those that show no visible reaction. From comparing test products in figures 1 and 2 test, it appears that test product 2425.07 has slightly more subjects who report erythema. Although 12 subjects did not complete the test for 2425.002 beyond day 15, while only 8 failed to complete the study with 2425.07 beyond day 14. Test substance 2425.02 induced skin damage (+D) in 3 subjects on day 13, while only 1 subject exposed to 2425.07 experienced skin damage (+D) on day 13. The test products appear to be mild compared to SLS, however. SLS appears to cause erythema faster and produce damage to the tissue. So much that the study could not be continued after day 9.

C. **POSITIVE CONTROL**: SLS was used as a positive control in this study.

III. DISCUSSION

A. **INVESTIGATOR'S CONCLUSIONS**: Thirty subjects between the ages of 32 and 73 were enrolled and 24 completed the study, which deviates from the protocol requirement of 25 subjects. Of the thirty subjects enrolled, five subjects were voluntarily withdrawn

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and one was removed because of a protocol violation (e.g., the subject removed patches). There were no adverse effects reported for these individuals. The study provides irritation scores and classification schemes, which are outlined in Table 3 (presented previously).

B. REVIEWER'S DISCUSSION/CONCLUSIONS:

The investigator's conclusions seem appropriate from the results. The negative and positive controls had irritation scores as expected. However, the actual active ingredients or concentrations were not reported. Several other deficiencies with the study are noted below.

C. DEFICIENCIES: The study was classified as **Unacceptable/Non-guideline** for the following deficiencies: 1) Complete lack of information regarding the active ingredient and purity of the test material. 2) The study was **not** conducted in accordance with EPA Good Laboratory Practices (GLPs). 3) The Protocol specifies that 30 subject be tested and only 24 made it through the completion of the study. 4) No protocol documentation was provided.

D. STUDY CLASSIFICATION: This study is classified as **Unacceptable/Non-guideline** (upgradable) because of the deficiencies noted above.

New York State Department of Environmental Conservation
Division of Solid & Hazardous Materials
Bureau of Pesticides Management
Pesticide Product Registration Section
625 Broadway, Albany, New York 12233-7257
Phone 518-402-8768 **FAX** 518-402-9024
Website: http://www.dec.state.ny.us/website/dshm/pesticid/pesticid.htm
E-Mail: ppr@gw.dec.state.ny.us

Erin M. Crotty
Commissioner

CERTIFIED MAIL

RETURN RECEIPT REQUESTED

January 23, 2004

Mr. Eliot Harrison
Agent for Kimberly-Clark Corporation
c/o Lewis & Harrison, LLC
122 C Street NW
Suite 740
Washington, DC 20001

Dear Mr. Harrison:

Re: Intent to Deny Application to Register Kleenex Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-10)

The New York State Department of Environmental Conservation (Department) received your application to register Kleenex Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-10) on October 3, 2003. The product application was declared administratively complete and the application package has been reviewed in accordance with New York State and federal pesticide labeling guidance. The Department intends to deny this product application unless the following label issues can be resolved.

The final product labeling complies with the United States Environmental Protection Agency (USEPA) stamped "ACCEPTED" label dated 08/21/2003. However, the use directions are located on the bottom panel of the package and may not be apparent to the consumer when purchasing the product. In order that consumers purchasing this product in New York State are aware that the anti-viral claim refers to the killing of labeled viruses on the tissue after a 15-minute contact time, the Department suggests that this information be prominently displayed in proximity to the anti-viral claim on the principal display panel. The Department believes that, without the above clarification, the product name "Kleenex Brand Anti-Viral™" could be construed by the consumer to mean anti-viral during the time of use (certainly not a 15-minute duration) of the tissue by the cold or flu sufferer.

Additionally, the Department has concerns about the first statement on the back panel of the label, "A leading cause of the spread of cold and flu viruses is by hand contact." Although true, the Department believes this statement can lead a consumer to assume that the Kleenex Brand Anti-Viral™ tissue acts to control the spread of cold and flu viruses more than a tissue of similar physical characteristics. Please refer to 40 CFR Part 156.10(a)(5)(vii) under "False and misleading statements" which states that "a pesticide is misbranded if its labeling is false or misleading in any particular including both pesticidal and non-pesticidal claims."

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New York State Department of Environmental Conservation
Division of Solid & Hazardous Materials
Bureau of Pesticides Management
Pesticide Product Registration Section
625 Broadway, Albany, New York 12233-7257
Phone 518-402-8768 **FAX** 518-402-9024
Website: http://www.dec.state.ny.us/website/dshm/pesticid/pesticid.htm
E-Mail: ppr@gw.dec.state.ny.us

Erin M. Crotty
Commissioner

CERTIFIED MAIL

RETURN RECEIPT REQUESTED

January 23, 2004

Mr. Eliot Harrison
Agent for Kimberly-Clark Corporation
c/o Lewis & Harrison, LLC
122 C Street NW
Suite 740
Washington, DC 20001

Dear Mr. Harrison:

Re: Intent to Deny Application to Register Kleenex Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-10)

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(24)

40 CFR Part 156.10(a)(5)(vii) "A true statement used in such a way as to give a false or misleading impression to the purchaser."

In lieu of removing this statement, the Department would review any USEPA accepted studies which demonstrate that Kleenex Brand Anti-Viral™ tissue acts to control the spread of cold and flu viruses more than a tissue of similar characteristics.

The Department also requested comment on the product and its label from the New York State Department of Health (NYSDOH). NYSDOH agreed that the label claims appear inappropriately placed and are misleading given the customary use of tissues. In addition, NYSDOH expressed the generic concern that unnecessarily using antimicrobial agents in so many household products could potentially increase the resistance of microorganisms to antimicrobials/antibiotics and reduce efficacy. This is of particular concern for the Kleenex Brand AntiViral™ tissues given the apparent lack of any health benefit they confer to the user. Please address these concerns in your response.

Within 30 days from receipt of this letter, you may make the necessary changes and/or submit the documentation requested above. If you do not submit the requested documentation, or if you submit the requested documentation and there are still deficiencies in your application, the review will be terminated and your application for registration will be denied.

If Kimberly-Clark Corporation has prepared product labeling based on a more current USEPA stamped "Accepted" label or notification than specified above, three copies of this labeling and a copy of the supporting document must be submitted.

The Department takes this action because New York State will not register labels that:

1. Are inconsistent with the most current USEPA stamped "Accepted" labels or variations allowed by 40 CFR Sections 152.130 and 152.132 or
2. Contain false or misleading statements as indicated in 40 CFR Part 156.10(a)(5).

Please be aware that any unregistered product may **not** be sold, offered for sale, distributed, or used in New York State.

Should you have any questions regarding this letter please contact Paula McBath, of my staff, at (518) 402-8768.

Sincerely,

Samuel J. Jackling
Chief
Pesticide Product Registration Section

cc: - Adam Heyward, Product Manager 34; Regulatory Management Branch II; Antimicrobials Division; Office of Pesticide Programs; USEPA
- Connie Welch, Branch Chief; Regulatory Management Branch II; Antimicrobials Division; Office of Pesticide Programs; USEPA

(40)

458702-00

LEWIS & HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

February 26, 2003

Document Processing Desk - 6(a)(2)
Office of Pesticide Programs - 7504 (c)
U.S. Environmental Protection Agency
Crystal Mall #2
Arlington, VA 22202
attn: Adam Heyward, Product Manager (34)

re: Reportable Information Under FIFRA Section 6(a)(2)
Product: Kleenex® Brand Anti-Viral Tissue #2
EPA File Symbol No. 9402-RE
Active Ingredients: Citric Acid and Sodium Lauryl Sulfate

Dear Mr. Heyward:

On behalf of Kimberly-Clark Corporation, I am submitting pursuant to Section 6(a)(2) of FIFRA and EPA's regulations at 40 C.F.R. Part 159, a human clinical dermal study conducted with Kleenex® Brand Anti-Viral Tissue #2. A registration application for this product is currently pending with the Agency's Antimicrobial Division, Office of Pesticide Programs (AD/OPP). As discussed further below, Kimberly-Clark is confident that Kleenex® Brand Anti-Viral Tissue #2 is not a dermal irritant when used, as intended, as a facial tissue.

To support the registration of Kleenex® Brand Anti-Viral Tissue #2, Kimberly-Clark conducted a dermal irritation study in rabbits (OPPTS Guideline No. 870.2500). No irritation was observed in any of the test animals. Accordingly, Kleenex® Brand Anti-Viral Tissue #2 has been classified as non-irritating to skin. Separate from the dermal irritation study required by OPP for product registration, Kimberly-Clark, as do most other consumer product companies, conducted human clinical studies to evaluate whether Kleenex® Brand Anti-Viral Tissue #2 may cause either cumulative irritant contact dermatitis and/or allergic contact dermatitis. These human studies were performed under conditions that simulate both the intended use and potential significant misuse, of the Kleenex® Brand Anti-Viral Tissue #2.

(41)

The allergic contact dermatitis study (titled, "Repeated Insult Patch Study", No. DS106902-2) clearly demonstrated that Kleenex® Brand Anti-Viral Tissue #2, irrespective of the patching conditions employed, did not cause allergic contact dermatitis.

The cumulative irritant contact dermatitis study (titled, "21-Consecutive-Day Cumulative Irritation Patch Study", No. DS310502-1) was performed under conditions that can be considered much more severe than the standard animal dermal irritation study. For example, in the human study the test material (Kleenex® Brand Anti-Viral Tissue #2) was applied to each study participant for 23.5 consecutive hours per day for 21 consecutive days. In the animal study, the test material was placed under a semi-occlusive patch for 4 hours. The four different human testing conditions were:

- Semi-occlusive patching of dry tissue (simulates intended use);
- Semi-occlusive patching of wet tissue (simulates misuse);
- Occlusive patching of dry tissue (simulates significant misuse); and
- Occlusive patching of wet tissue (simulates significant misuse).

It is important to emphasize that occlusive patching was employed in order to evaluate potential significant product misuse, such as feminine hygiene use as a temporary tampon substitute or temporary occluded pad substitute.

Under conditions that simulated the intended use of Kleenex® Brand Anti-Viral Tissue #2 (semi-occlusive patch of dry test material/tissue), no irritation was observed in the study. Even under more severe test conditions (semi-occlusive patching of wet test material/tissue) the result was considered no different than the semi-occlusive patch with dry test material/tissue. Under conditions that simulated significant product misuse, moderate irritation was observed. However, even then, irritation was not seen until five days into the 21 day cumulative test. Thus, irritation would only occur if the misuse were both significant and continued for a longer period of time than could reasonably be expected for this product. Moreover, any irritation that did occur to the test participants during the study, dissipated after use of the test material/tissue was discontinued, and there was no permanent damage to the underlying dermis.

Based on the results of the human studies, Kimberly-Clark is confident that Kleenex® Brand Anti-Viral Tissue #2, is not a dermal irritant when used as intended, as a facial tissue. Consistent with EPA packaging/labeling requirements, the package label will clearly indicate "For use only as a facial tissue".

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If you have questions about this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

February 26, 2003

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RE
Applicant: Kimberly-Clark Corporation
Registration Application for New Product
Data Transmittal Letter for Studies being Submitted in Response to Your Correspondence of November 25, 2002

Dear Adam:

On behalf of Kimberly-Clark Corporation, I am submitting the following studies pursuant to FIFRA 6(a)(2):

- Volume 1 of 2
  21-Consecutive-Day Cumulative Irritation Patch Study
  MRID# 45870201

- Volume 2 of 2
  Repeated Insult Patch Study
  MRID# 45870202

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

February 11, 2004

Eliot I. Harrison
Lewis & Harrison Consultants, Agent for
Kimberly-Clark Corp.
122 C Street, N.W., Suite 740
Washington, DC 20001

Subject: **Kleenex® Brand Anti-Viral™ Tissue**
EPA Registration No. 9402-10
Letter Dated January 12, 2004

Dear Mr. Harrison:

The following amendments, submitted in connection with registration under section 3(c)(7)(A) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, are acceptable.

Proposed Amendment:

- Change official brand name to Kleenex® Brand Anti-Viral Tissue
- The claim "Kills 99.9% of Cold and Flu Viruses" has been added to the front panel
- On the back panel, the heading and the descriptive paragraph has been changed
- Revise Directions for Use
- Add asterisk after all references to the term "anti-viral".

General Comment:

A stamped copy of the accepted labeling is enclosed.

Should you have any questions or comments concerning this letter, please contact me at (703) 308-6422 or Renae Whitaker at (703) 308-7003.

Sincerely,

Adam Heyward
Product Manager (34)
Regulatory Management Branch II
Antimicrobials Division (7510C)

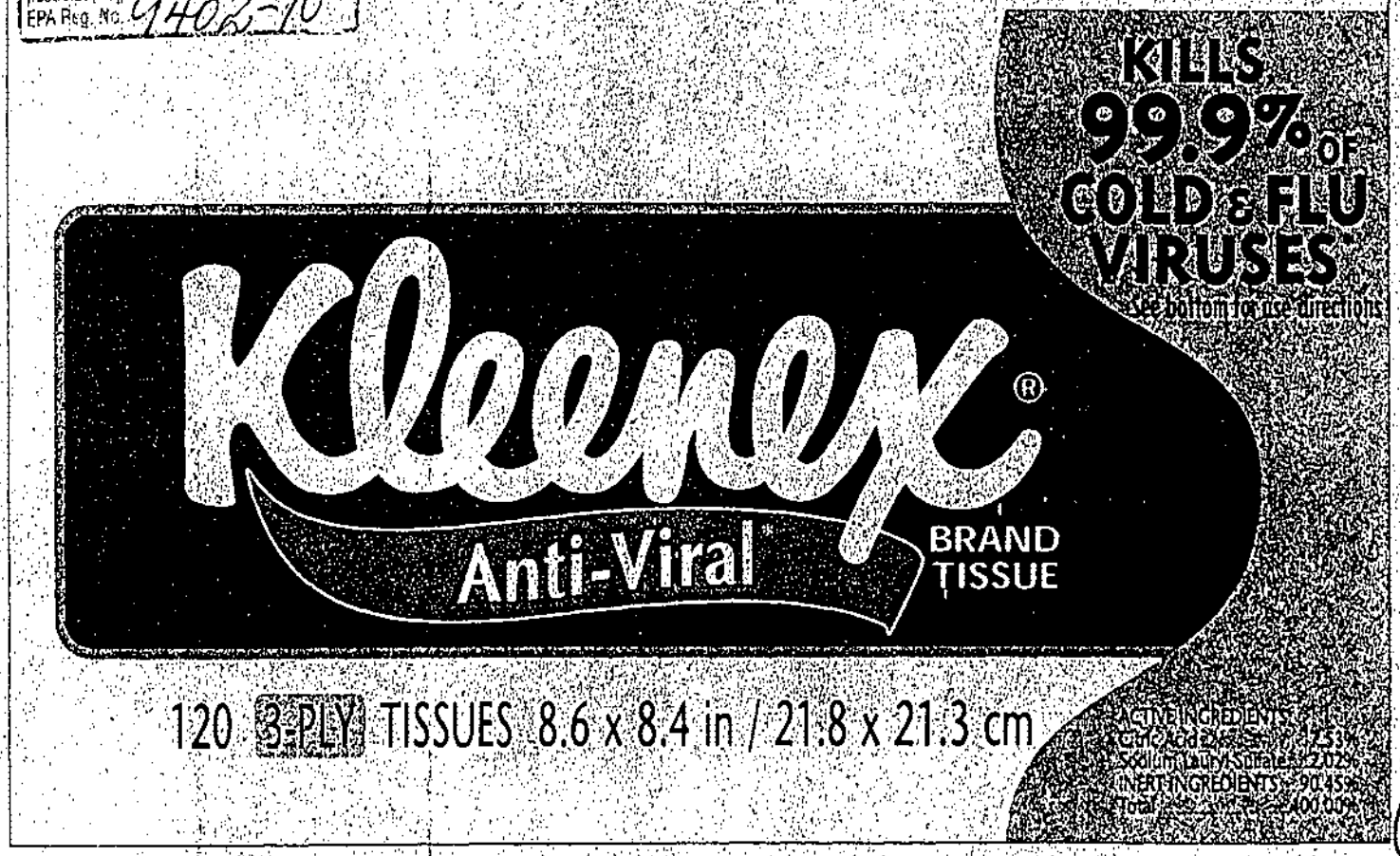
Enclosure

CONCURRENCES							
SYMBOL							
SURNAME							
DATE							

EPA Form 1320-1A (1/90) *Printed on Recycled Paper* OFFICIAL FILE COPY

*U.S. Government Printing Office: 1992 — 820-856/40067

ACCEPTED
FEB 11 2004
Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide, registered under EPA Reg. No. 9402-10



46

New KLEENEX® Anti-Viral tissue kills 99.9% of Cold and Flu Viruses**

Because cold and flu viruses are often spread by hand contact, KLEENEX® Brand has developed a new tissue for your whole family. New! KLEENEX® Anti-Viral* tissue has three soft layers, including a moisture-activated middle layer that kills 99.9% of cold and flu viruses* in the tissue within 15 minutes. This product has not been tested against bacteria, fungi or other viruses. See below for anti-viral* details.

Kleenex® Anti-Viral BRAND TISSUE

LOOKING GLASS FPO

Directions for Use: It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Use only as a facial tissue.

*Virucidal Against: Rhinoviruses Type 1A and 2 (Rhinoviruses are the leading cause of the common cold); Influenza A and Influenza B (causes of the flu); Respiratory Syncytial Virus (RSV–the leading cause of lower respiratory infection in children).

Storage and Disposal: Store in a dry area. Dispose of used tissues promptly. Do not reuse empty container.

1-800-553-3639 weekdays 8 a.m. to 4 p.m. CT

Distributed by Kimberly-Clark Global Sales, Inc.,
Dept. KAV-120, PO Box 2020, Neenah, WI 54957-2020
Printed in USA.
Made in the USA from domestic and imported material.

www.kleenex.com

® Registered Trademark of Kimberly-Clark Worldwide, Inc.
© 1938, 1986, 2004 KCWW
Made under the following US patents:
6,221,211; 5,227,242; 4,828,912; 4,738,847.

120 3-PLY TISSUES 8.6 X 8.4 IN

This box is made from 100% recycled paper.

ACTIVE INGREDIENTS:

Citric Acid	7.53%
Sodium Lauryl Sulfate	2.02%
INERT INGREDIENTS	90.45%
Total	100.00%

EPA Reg. No.: 9402-10
EPA Est. No.: 009402-SC-001

ACCEPTED
FEB 11 2004
Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide, registered under EPA Reg. No.

47

LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

February 11, 2004

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-10
Registrant: Kimberly-Clark Corporation
Pending Label Amendment

Dear Adam:

As we discussed earlier today, please find enclosed five (5) revised copies of the amended label for Kleenex® Brand Anti-Viral Tissue #2. The revisions, which are very minor, are those requested by the New York State Department of Environmental Conservation. Please refer to the attached note from me to Sam Jackling regarding the specific revisions. In addition, we are requesting that the official name of the product be changed from Kleenex® Brand Anti-Viral Tissue #2 to Kleenex® Brand Anti-Viral Tissue.

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

48

Eliot I. Harrison

From: Sam Jackling [sjjackli@gw.dec.state.ny.us]
Sent: Tuesday, February 10, 2004 10:36 AM
To: eharrison@lewisharrison.com
Subject: Re: Kleenex Anti-Viral

Eliot,
On the bottom of the large tissue box it states:
New Kleenex Anti-Viral tissue kills 99.9% of Cold and Flu Viruses*.
The term Anti-Viral does not have an *.
As we agreed, every instance of the term "Anti-Viral" should have an *.
I know the * is at the end of the sentence but we believe it should
also be after the term Anti-Viral in this sentence.

Assuming this change is made, DEC agrees that you have addressed our concerns. As you are aware we cannot give final approval until we review the final EPA "Accepted" label. Upon receipt of a EPA "Accepted" label we will attempt to complete the review within 1-2 weeks.

Sam Jackling

amuel J Jackling
Chief, Pesticide Product Registration Section
New York State Department of Environmental Conservation
625 Broadway
Albany, NY 12233-7257

(518) 402-8768
(518) 402-9024 (fax)

>>> "Eliot Harrison" <eharrison@lewisharrison.com> 02/08/04 01:23PM
>>>
Hi Sam,
Attached is the follow-up material we discussed at our meeting on Tuesday.
The hard copies will be sent by overnight delivery on Monday.
Regards,
Eliot

49

To: Samuel J. Jackling
From: Eliot Harrison
Re: Kleenex Brand Anti-Viral Tissue

On behalf of Kimberly-Clark Corporation (K-C), I want to thank you, Paula McBath and Jeanine Broughel for meeting with us on Tuesday, February 3, 2004 to discuss issues regarding the NYSDEC registration of Kleenex® Brand Anti-Viral Tissue. K-C respresentatives attending the meeting were Steve Erb, Kevin Eberle, Michael Caringello, Christopher McKenzie and myself.

At the meeting, we discussed in detail the labeling concerns expressed in your letter of January 23, 2004. It is our understanding that agreement was reached to modify the label as follows:

- On the principal display panel, after the phrase "KILLS 99.9% OF COLD & FLU VIRUSES," the phrase "See bottom panel for details" will be replaced with the phrase "See bottom for use directions." In addition, the font size for this instruction will be increased to make it more prominent.
- An asterisk will be inserted after all references to the term "anti-viral" on the principal display panel and bottom panel of the tissue box (but not on the poly window covering the dispensing area of the box, on which the word "Anti-Viral" is printed repeatedly as a watermark). The asterisk will direct consumers to the use directions on the bottom panel. Note that the asterisk after the words "COLD & FLU VIRUSES" will be retained to direct consumers to the explanation on the bottom panel of which cold and flu viruses are targeted.
- Finally, as a point of clarification, the symbol "#2" will not be included as part of the product name. Similarly, the active ingredients will, of course, be displayed prominently on the principal display panel (active ingredients were inadvertently not included on one of the labels provided to you at the meeting), as well as on the bottom panel.

Attached hereto is a revised label (pdf file) incorporating the above label changes. A hard copy of the revised label will be sent by overnight courier. We request your prompt concurrence with the revised label.

Following NYSDEC concurrence, we will immediately forward to USEPA the final proposed label, as revised, and will provide a copy to NYSDEC. As soon as USEPA approval is obtained, we will submit the final approved label to NYSDEC to obtain New York state registration approval. NYSDEC has informed us that it will endeavor to process such request in approximately 1-2 weeks.

Once again, thank you for taking the time to meet with us. Please contact me at 202-393-3903, ext 14 if you have questions or require any additional information.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

January 30, 2004

MEMORANDUM:

Subject: Efficacy Review EPA Reg. 9410-10 *Kleenex Brand Anti-Viral Tissue*
DP Barcode 298261

From: Nancy Whyte, Microbiologist NW
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

To: Adam Heyward/Renae Whitaker
Regulatory Management Branch I
Antimicrobials Division (7510C)

Thru: Emily Mitchell, M.S., Team Leader
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

Thru: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Applicant: Kimberly-Clark Corporation
PO Box 2020
Neenah, WI 54957-2020

Formulation Label:

Active Ingredient(s)	**%/wt**
Citric acid	7.53%
Sodium lauryl sulfate	2.02%
Other ingredients	90.45%
Total	100.00%

I. Background:

This label from the registrant's consultant was submitted for amendment. The changes made to the label required by the Agency as a condition of registration, are acceptable.

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New York State Department of Environmental Conservation
Division of Solid & Hazardous Materials
Bureau of Pesticides Management
Pesticide Product Registration Section
625 Broadway, Albany, New York 12233-7257
Phone 518-402-8768 **FAX** 518-402-9024
Website: http://www.dec.state.ny.us/website/dshm/pesticid/pesticid.htm
E-Mail: ppr@gw.dec.state.ny.us

Erin M. Crotty
Commissioner

CERTIFIED MAIL

RETURN RECEIPT REQUESTED

January 23, 2004

Mr. Eliot Harrison
Agent for Kimberly-Clark Corporation
c/o Lewis & Harrison, LLC
122 C Street NW
Suite 740
Washington, DC 20001

Dear Mr. Harrison:

Re: Intent to Deny Application to Register Kleenex Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-10)

The New York State Department of Environmental Conservation (Department) received your application to register Kleenex Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-10) on October 3, 2003. The product application was declared administratively complete and the application package has been reviewed in accordance with New York State and federal pesticide labeling guidance. The Department intends to deny this product application unless the following label issues can be resolved.

The final product labeling complies with the United States Environmental Protection Agency (USEPA) stamped "ACCEPTED" label dated 08/21/2003. However, the use directions are located on the bottom panel of the package and may not be apparent to the consumer when purchasing the product. In order that consumers purchasing this product in New York State are aware that the anti-viral claim refers to the killing of labeled viruses on the tissue after a 15-minute contact time, the Department suggests that this information be prominently displayed in proximity to the anti-viral claim on the principal display panel. The Department believes that, without the above clarification, the product name "Kleenex Brand Anti-Viral™" could be construed by the consumer to mean anti-viral during the time of use (certainly not a 15-minute duration) of the tissue by the cold or flu sufferer.

Additionally, the Department has concerns about the first statement on the back panel of the label, "A leading cause of the spread of cold and flu viruses is by hand contact." Although true, the Department believes this statement can lead a consumer to assume that the Kleenex Brand Anti-Viral™ tissue acts to control the spread of cold and flu viruses more than a tissue of similar physical characteristics. Please refer to 40 CFR Part 156.10(a)(5)(vii) under "False and misleading statements" which states that "a pesticide is misbranded if its labeling is false or misleading in any particular including both pesticidal and non-pesticidal claims."

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40 CFR Part 156.10(a)(5)(vii) "A true statement used in such a way as to give a false or misleading impression to the purchaser."

In lieu of removing this statement, the Department would review any USEPA accepted studies which demonstrate that Kleenex Brand Anti-Viral™ tissue acts to control the spread of cold and flu viruses more than a tissue of similar characteristics.

The Department also requested comment on the product and its label from the New York State Department of Health (NYSDOH). NYSDOH agreed that the label claims appear inappropriately placed and are misleading given the customary use of tissues. In addition, NYSDOH expressed the generic concern that unnecessarily using antimicrobial agents in so many household products could potentially increase the resistance of microorganisms to antimicrobials/antibiotics and reduce efficacy. This is of particular concern for the Kleenex Brand AntiViral™ tissues given the apparent lack of any health benefit they confer to the user. Please address these concerns in your response.

Within 30 days from receipt of this letter, you may make the necessary changes and/or submit the documentation requested above. If you do not submit the requested documentation, or if you submit the requested documentation and there are still deficiencies in your application, the review will be terminated and your application for registration will be denied.

If Kimberly-Clark Corporation has prepared product labeling based on a more current USEPA stamped "Accepted" label or notification than specified above, three copies of this labeling and a copy of the supporting document must be submitted.

The Department takes this action because New York State will not register labels that:

1. Are inconsistent with the most current USEPA stamped "Accepted" labels or variations allowed by 40 CFR Sections 152.130 and 152.132 or
2. Contain false or misleading statements as indicated in 40 CFR Part 156.10(a)(5).

Please be aware that any unregistered product may **not** be sold, offered for sale, distributed, or used in New York State.

Should you have any questions regarding this letter please contact Paula McBath, of my staff, at (518) 402-8768.

Sincerely,

Samuel J. Jackling
Chief
Pesticide Product Registration Section

cc: - Adam Heyward, Product Manager 34; Regulatory Management Branch II; Antimicrobials Division; Office of Pesticide Programs; USEPA
- Connie Welch, Branch Chief; Regulatory Management Branch II; Antimicrobials Division; Office of Pesticide Programs; USEPA

EPA United States Environmental Protection Agency

Office of Pesticide Programs

State Label Issue Tracking System

Requester: Paula McBath (pjmcbath@gw.dec.state.ny.us)
Entity/Affiliation: New York

Request Date: 01/15/2004
Due Date: 01/19/2004

Product #: 009402-00010
Product Name: KLEENEX BRAND ANTI-VIRAL TISSUE #2
PC Codes: 021801 Citric Acid
079011 Sodium Lauryl Sulfate
OPP Team: RM 34
Risk Manager: Adam Heyward

Subject: Label Clarification
Brief Desc: Anti-viral claims may be true statements but are misleading to the consumer
Detailed Desc: New York State is reviewing the above product labeling for registration and find that the product labeling may mislead the consumer to believe that the tissue would kill germs during the "use" phase. The first statement on the label is "A leading cause of the spread of cold and flu viruses is by hand contact." The label then states that the "moisture activated middle layer kills 99.9% of cold and flu viruses in the tissue within 15 minutes." Thus a consumer skimming this label may think that this tissue will kill germs while the user is handling the tissue. In reality it takes 15 minutes to kill these germs which would place the tissue somewhere in a trash can and out of the user's hands. [False and misleading statements per 40 CFR Part 156.10(a)(5)(vii)] Thus a true statement can be used in such a way to provide a false and misleading view to the purchaser of this product.

We believe that the consumer should be notified by prominent display on the front panel of the tissue box that this anti-viral claim refers to the killing of viruses on the tissue after a fifteen minute exposure time. Please advise....

Also, in regard to the hand contact and transfer of viruses - Were there any comparative studies to determine if there was any reduction in germ transfer by hand contact with the Anti-viral Kleenex vs. an equal strength tissue without the active ingredients? It would seem that without such information the whole premise of registering this product is leading to an overload of antimicrobials for every conceivable household use thus leading to potential increased resistence by common micro-organisms and the consequent loss of effective controls - just a thought.

Attach File(s):

Respond | Acknowledge | Close

EPA Home | Search EPA | Comments | Site Map
OPP Home | Search OPP | State Label Issue Tracking Registration System | Search for Product Label
Search State Label Issue Tracking System | Contact System Administrator | User Manual

http://yosemite.epa.gov/opp/opp_label_request.nsf
Version 2.0, updated 09/26/2003

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 16, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

ELIOT HARRISON
LEWIS & HARRISON, AGENT FOR
KIMBERLY-CLARK CORP
LEWIS & HARRISON, LLC
122 C ST., N.W., SUITE 740
WASHINGTON, D.C. 20001

PRODUCT NAME: KLEENEX BRAND ANTI-VIRAL TISSUE #2
COMPANY NAME: KIMBERLY-CLARK CORP
OPP IDENTIFICATION NUMBER: 256737
EPA FILE SYMBOL: 9402-10
EPA RECEIPT DATE: 01/16/04

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Antimicrobials Division, Risk Management Team 34, at (703) 308-6422.

Sincerely,

J Wroe

Front End Processing Staff
Information Services Branch
Information Resources and Services Division

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LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

January 12, 2003

Adam Heyward, Product Manager (34)
Regulatory Management Branch No. II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway
Crystal Mall #2
Arlington, VA 22202

re: **Kleenex® Brand Anti-Viral™ Tissue #2**
EPA Reg. No. 9402-10
Registrant: Kimberly-Clark Corporation
Label Amendment

Dear Adam:

On behalf of Kimberly-Clark Corporation, I am submitting a label amendment for Kleenex® Brand Anti-Viral Tissue #2. The amendment proposes to amend the currently approved label as follows:

1) The official brand name of the product has been changed from Kleenex® Brand Anti-Viral Tissue #2 to Kleenex® Brand Anti-Viral Tissue.

2) The claim "Kills 99.9% of Cold and Flu Viruses" has been added to the front panel.

3) On the back panel, the heading for the descriptive paragraph has been changed from "The soft tissue now kills cold and flu viruses" to "New Kleenex® Anti-Viral tissue kills 99.9% of cold and flu viruses".

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4) The descriptive paragraph has been changed from:

"A leading cause of the spread of cold and flu viruses is by hand contact. Now Kleenex® Brand gives you a soft, anti-viral tissue with a special moisture-activated middle layer scientifically proven to kill 99.9% of cold and flu viruses in the tissue within 15 minutes. This product has not been tested against bacteria, fungi or other viruses. Especially designed for the whole family. Try new Kleenex® Brand Anti-Viral Tissue #2 today."

to

" Because cold and flu viruses are often spread by hand contact, Kleenex® Brand has developed a new tissue for your whole family. New! Kleenex® Anti-Viral Tissue has three soft layers, including a moisture-activated middle layer that kills 99.9% of cold and flu viruses in the tissue within 15 minutes. This product has not been tested against bacteria, fungi or other viruses. Try them today!"

5) In the "Directions for Use" the sentence "Use only as a facial tissue to prevent the spread of cold and flu viruses has been changed to "Use only as a facial tissue."

In support of this amendment, please find enclosed the following documents:

- Application for Pesticide Form.
- Proposed Product Label (5 Copies)

If you have any questions about this amendment, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark Corp.

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Please read instructions on reverse before completing form. Form Approved, OMB No. 2070-0060, Approval expires 05-31-98

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☐ **Registration**
☒ **Amendment**
☐ **Other:**

OPP Identifier Number
256737

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
9402-10	Adam Heyward	☒ None ☐ Restricte
4. Company/Product (Name)	PM#	
Kleenex® Brand Anti-Viral Tissue #2	Team 34	

5. Name and Address of Applicant *(Include ZIP Code)*
Kimberly-Clark Corporation
2100 Winchester Road
Neenah, WI 54956
PLEASE DIRECT ALL CORRESPONDENCE TO "CONTACT POINT" LISTED BELOW
☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

Section - II

☒ Amendment – Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application
☐ Other - Explain below

Explanation: Use additional page(s) if necessary. (For Section I and Section II.)

APPLICATION FOR LABEL AMENDMENT. SEE COVER LETTER FOR DETAILS.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes*	☐ Yes	☐ Yes	☐ Metal
☐ No	☐ No	☐ No	☐ Plastic
	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt. / No. per container	☐ Glass
			☐ Paper
			☐ Other (Specify)

***Certification must be submitted**

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ Container		☐ On Label ☐ On labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application)*

Name	Title	Telephone No. (Include Area Code)
Eliot Harrison, Lewis and Harrison, LLC 122 C St., NW Suite 740 Washington, DC 20001	Agent for Kimberly-Clark Corporation	(202) 393-3903 x 17

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature	3. Title: Agent for Kimberly-Clark Corporation	6. Date Application Received (Stamped)
Eliot Harrison		58
4. Typed Name: Eliot Harrison, *Lewis & Harrison LLC*	5. Date: 1/12/04	

EPA RQ#9402-10

Page____ is not included in this copy.

Pages 59 through 64 are not included.

The material not included contains the following type of information:

✓ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

✓ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Please Expedite

PM WORK ASSIGNMENT SHEET

DECISION _____ PM 34

DESCRIPTION OF ACTION: _____

SUBMISSION BAR CODE: S 750488

PRODUCT REVIEWER: Renee

FILE SYMBOL/REG NO.: 9402-10

FQPA ACTION CODE: 332 NON-FQPA ACTION CODE: _____

AMOUNT OF TIME TO COMPLETE TASK (**ASRC** only)	HOURS _____

	MONTH	DAY	YEAR
APPLICATION DATE	10	29	03
EPA PIN DATE	10	29	03
REVIEWER ASSIGNED DATE	11	21	03
DATE DUE OUT OF AGENCY	11	25	03

TYPE OF DATA

Product Chemistry: ☐ **Product Toxicology:** ☐ **Efficacy:** ☐

RASSB: ☐ **HED TOX** ☐ **ENVIRONMENTAL FATE** ☐ **FISH/WILDLIFE** ☐

Other ☐ _____

COMMENTS:

_____

_____

_____

_____

_____

_____

JACKET(S)/FILE SHOULD BE SUBMITTED WITH YOUR LETTERS FOR SIGNATURE

RESPONSE CODE: 17 RESPONSE DATE: ~~11~~ 11 / 25 / 03
MO Day Year

(05)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

November 25, 2003

Georgia Anastasiou,
Lewis and Harrison Consultants
Agent for Kimberly Clark Corporation
122 C Street
Washington, DC 20001

Subject: Notification in Accordance with PR Notice 98-10
Kleenex Brand Anti-Viral Tissue #2
EPA Registration Number 9402-10
Application dated October 28, 2003

Dear Ms. Anastasiou:

This will acknowledge receipt of your notification, submitted under the provisions of PR Notice 98-10, FIFRA section 3 (c) 9.

Proposed Notifications:

Alternate Brand Name

- Kleenex Brand Anti-Viral Tissue

General Comment:

Based on a review of the material submitted, the following comment apply.

The notification application is acceptable. A copy have been inserted in your file for future reference.

Should you have any questions or comments concerning this letter, please contact me at (703) 308-6422 or Renae Whitaker at (703) 308-7003.

Sincerely,

Renae L. Whitaker

Adam Heyward
Product Manager 34
Regulatory Management Branch II
Antimicrobials Division (7510C)

CONCURRENCES

SYMBOL								
SURNAME								
DATE								

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LEWIS & HARRISON
Consultants In Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

HAND DELIVERED

October 29, 2003

Document Processing Desk (NOTIF)
Office of Pesticide Programs
U.S. Environmental Protection Agency (7504C)
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

ATTENTION: **Velma Noble**
Product Manager, Team 31

SUBJECT: ***Kimberly-Clark Corporation***
Kleenex Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-10)
Notification of Alternate Brand Name Per PR Notice 98-10

Dear Ms. Noble:

On behalf of Kimberly-Clark Corporation, we are submitting an application for Pesticide Notification to propose an alternate brand name for **Kleenex Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-10)** in accordance with PR Notice 98-10. The alternate brand name for **Kleenex Brand Anti-Viral Tissue #2** is the following:

"Kleenex Brand Anti-Viral Tissue"

To support this Notification of Alternate Brand Name, we are submitting an Application for Pesticide Notification (OPP ID No. 265394), which includes a signed statement certifying compliance with PR Notice 98-10.

Insofar as Lewis & Harrison serves as the "Company Contact" and "Company Agent" for Kimberly-Clark, please relay all correspondence regarding this notification submission directly to us. If you have any questions, please contact me at (202) 393-3903 ext. 19 or e-mail me at georgia@lewisharrison.com

I thank you in advance for your cooperation.

Sincerely,

Georgia Anastasiou
Agent for Kimberly-Clark Corporation

Enclosures

cc: Michael Caringello (KCC)

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Please read instructions on reverse before completing form. Form Approved, OMB No. 2070-0060, Approval expires 05-31-98

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☐ Registration
☐ Amendment
☒ Other: Notification

OPP Identifier Number
265394

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
9402-10	Velma Noble	☒ None ☐ Restricted
4. Company/Product (Name)	PM#	
Kleenex Brand Anti-Viral Tissue #2	Team 31	
5. Name and Address of Applicant *(Include ZIP Code)* Kimberly-Clark Corporation 2100 Winchester Road Neenah, WI 54956 ***PLEASE DIRECT ALL CORRESPONDENCE TO "CONTACT POINT" LISTED BELOW*** ☐ *Check if this is a new address*	6. **Expedited Review**. In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to: EPA Reg. No. _____ Product Name _____	

Section - II

☐ Amendment – Explain below.
☐ Resubmission in response to Agency letter dated _____
☒ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application
☐ Other - Explain below

Explanation: Use additional page(s) if necessary. (For Section I and Section II.)

ALTERNATE BRAND NAMES: "Kleenex Brand Anti-Viral Tissue"

Notification of ALTERNATE BRAND NAME in Accordance With PR Notice 98-10

This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46, and no other changes have been made to the labeling or the confidential statement of formula of this product. I understand that it is a violation of 18 U.S.C. Sec 1001 to willfully make any false statement to EPA. I further understand that if this notification is not consistent with the terms of PR Notice 95-2 and 40 CFR 152.46, this product may be in violation of FIFRA and I may be the subject to enforcement action and penalties under sections 12 and 14 of FIFRA.

Signature: _____ Date: _____

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes*	☐ Yes	☐ Yes	☐ Metal
☐ No	☐ No	☐ No	☐ Plastic
	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt. / No. per container	☐ Glass ☐ Paper ☐ Other (Specify)

***Certification must be submitted**

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ Container		☐ On Label ☐ On labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application)*

Name	Title	Telephone No. (Include Area Code)
Georgia Anastasiou, Lewis and Harrison 122 C St., NW Suite 740 Washington, DC 20001	Agent for Kimberly-Clark Corporation	(202) 393-3903 x. 19

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature	3. Title: Agent for Kimberly-Clark Corporation	6. Date Application Received (Stamped)
		68
4. Typed Name Georgia Anastasiou, Lewis & Harrison LLC	5. Date October 28, 2003	

SUBMISSION BAR CODE # S634969 REVIEWER A Copeland

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 9402-RN PM 34 ACTION CODE 187

DESCRIPTOR Submission of efficacy studies

[ ] CHILD RESISTANT PACKAGING: [ ] CERTIFICATION
[ ] NON-RESIDENTIAL USE ONLY
[ ] NOT APPLICABLE

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL

PROPOSED CLASSIFICATION: [ ] GENERAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
4 25 03	4 28 03	5 6 03

METHOD OF SUPPORT:
[ ] CITE ALL
[ ] SELECTIVE
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

FORMULATORS EXEMPTION
[ ] SUBMITTED
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER _____				

STATUS _____

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RESPONSE CODE 18 RESPONSE DATE 5/21/03

SUBMISSION BAR CODE # S634569 REVIEWER D. Copeland

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 9402-RN PM 34 ACTION CODE 187

DESCRIPTOR Additional materials submitted

[ ] CHILD RESISTANT PACKAGING: [ ] CERTIFICATION
[ ] NON-RESIDENTIAL USE ONLY
[ ] NOT APPLICABLE

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL

PROPOSED CLASSIFICATION: [ ] GENERAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
4 25 03	4 28 03	5 1 03

METHOD OF SUPPORT

[ ] CITE-ALL
[ ] SELECTIVE
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

FORMULATORS EXEMPTION

[ ] SUBMITTED
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER _____				

STATUS _____

RESPONSE CODE 38 RESPONSE DATE 8/21/03

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U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Antimicrobials Division (7510C)
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460-0001

NOTICE OF PESTICIDE:

X Registration
___ Reregistration
(Under FIFRA, as amended)

EPA Reg. Number:	Date of Issuance:
9402-10	August 21, 2003

Terms of Issuance:
Conditional

Name of Pesticide Product:
Kleenex® Brand Anti-Viral Tissue #2

Name and Address of Registrant (include ZIP Code):

Kimberly -Clark Corporation
2100 Winchester Road
Neenah, WI 54957

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above-named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A) provided that you:

1. Submit and/or cite all data required for registration of your product under FIFRA sec. 3(c)(5) when the Agency requires all registrants of similar products to submit such data; and submit acceptable responses required for registration of your product under FIFRA section 4.

2. Make the following label changes:

   a. Revise the EPA Registration Number to read, " EPA Reg. No. 9402-10."

Signature of Approving Official:

Adam Heyward
Product Manager 34
Regulatory Management Branch II
Antimicrobials Division (7510C)

Date:
August 21, 2003

EPA Form 8570-6

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b. The word *"NEW"* may only be used for six months after the product has been released for shipment and sale.

c. The child signal word "Caution" and statement "Keep Out of Reach of Children" have been waived based on 40 CFR § 156.66(b)(2).

Submit three (3) copies of the revised final printed label bearing the revisions prior to releasing this product for sale.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). Your release for shipment of the product bearing the amended labeling constitutes acceptance of these conditions.

A stamped copy of the label is enclosed for your records.

Sincerely,

Adam Heyward
Product Manager (34)
Regulatory Management Branch II
Antimicrobials Division (7510C)

Enclosure:

The soft tissue now kills cold and flu viruses†

A leading cause of the spread of cold and flu viruses is by hand contact. Now KLEENEX® Brand gives you a soft, anti-viral† tissue with a special moisture-activated middle layer scientifically proven to kill 99.9% of cold and flu viruses† in the tissue within 15 minutes. This product has not been tested against bacteria, fungi or other viruses. Especially designed for the whole family. Try new KLEENEX® Brand Anti-Viral™ Tissue #2 today.

Kleenex® Anti-Viral BRAND TISSUE #2

LOOKING GLASS FOR POSITION ONLY UPC

Directions for Use: It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Use only as a facial tissue to help prevent the spread of cold and flu viruses†.

†Virucidal Against: Rhinoviruses Type 1A and 2 (Rhinoviruses are the leading cause of the common cold); Influenza A and Influenza B (causes of the flu); Respiratory Syncytial Virus (RSV–the leading cause of lower respiratory infection in children).

Storage and Disposal: Store in a dry area. Dispose of used tissues promptly. Do not reuse empty container.

1-800-553-3639 weekdays 8 a.m. to 4 p.m. CT

Distributed by Kimberly-Clark Global Sales, Inc.,
Dept. XX-XX, PO Box 2020, Neenah, WI 54957-2020
Printed in USA.
Made in the USA from domestic and imported material.

www.kleenex.com

Made under the following US patents:
6,221,211; 5,227,242; 4,828,912; 4,736,847.

This box is made from 100% recycled paper.

EPA Reg. No.: XXXX-XXX
EPA Est. No.: XXXXX-XX-XX

ACTIVE INGREDIENTS:
Citric Acid 7.53%
Sodium Lauryl Sulfate 2.02%
INERT INGREDIENTS 90.45%
Total 100.00%

[120] 3-PLY TISSUES

13

ACTIVE INGREDIENTS:
Citric Acid 7.53%
Sodium Lauryl Sulfate 2.02%
INERT INGREDIENTS.....90.45%
Total 100.00%

New!
Kleenex®
Anti-Viral™ BRAND TISSUE #2

[120] 3-PLY TISSUES • 8.6 x 8.4 in / 21.8 x 21.3 cm

New!
Kleenex®
Anti-Viral™ BRAND TISSUE #2

Kleenex® BRAND TISSUE

2

Facial Tissue Product with Overwrap

Principal Display Panel

ACCEPTED
with COMMENTS
EPA Letter Dated:

AUG 21 2003

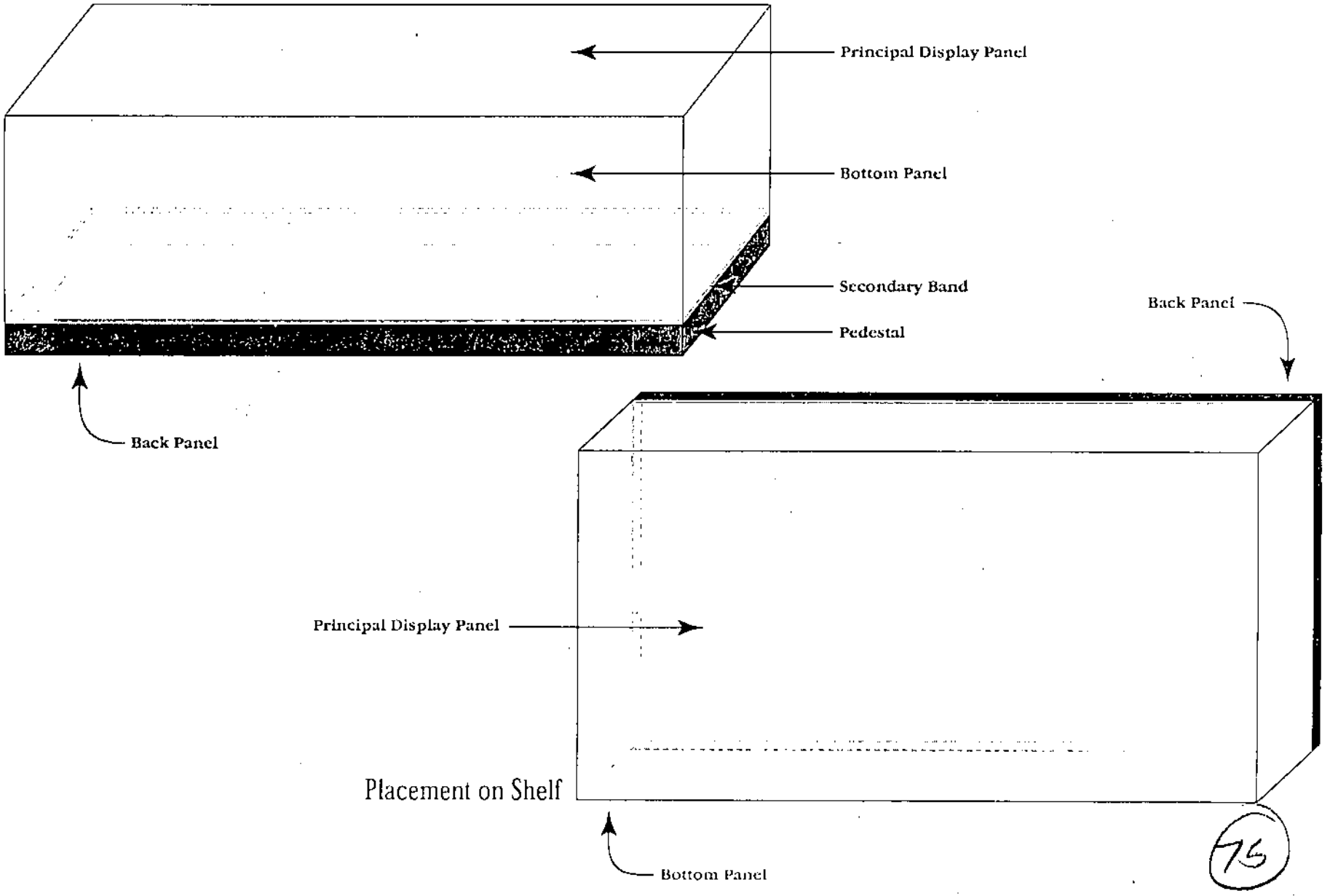
Under the Federal Insecticide, Fungicide, and Rodenticide Act as amended, for the pesticide, registered under EPA Reg. No.

9402-10

Bottom Panel

74

NOT TO SCALE


Principal Display Panel
Bottom Panel
Secondary Band
Pedestal
Back Panel
Back Panel
Principal Display Panel
Placement on Shelf
Bottom Panel
75

Facial Tissue Product with Overwrap

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Sodium Lauryl Sulfate 2.02%
INERT INGREDIENTS 90.45%
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New!
Kleenex®
Anti-Viral™ BRAND TISSUE #2

[120] 3-PLY TISSUES • 8.6 x 8.4 in / 21.8 x 21.3 cm

Principal Display Panel

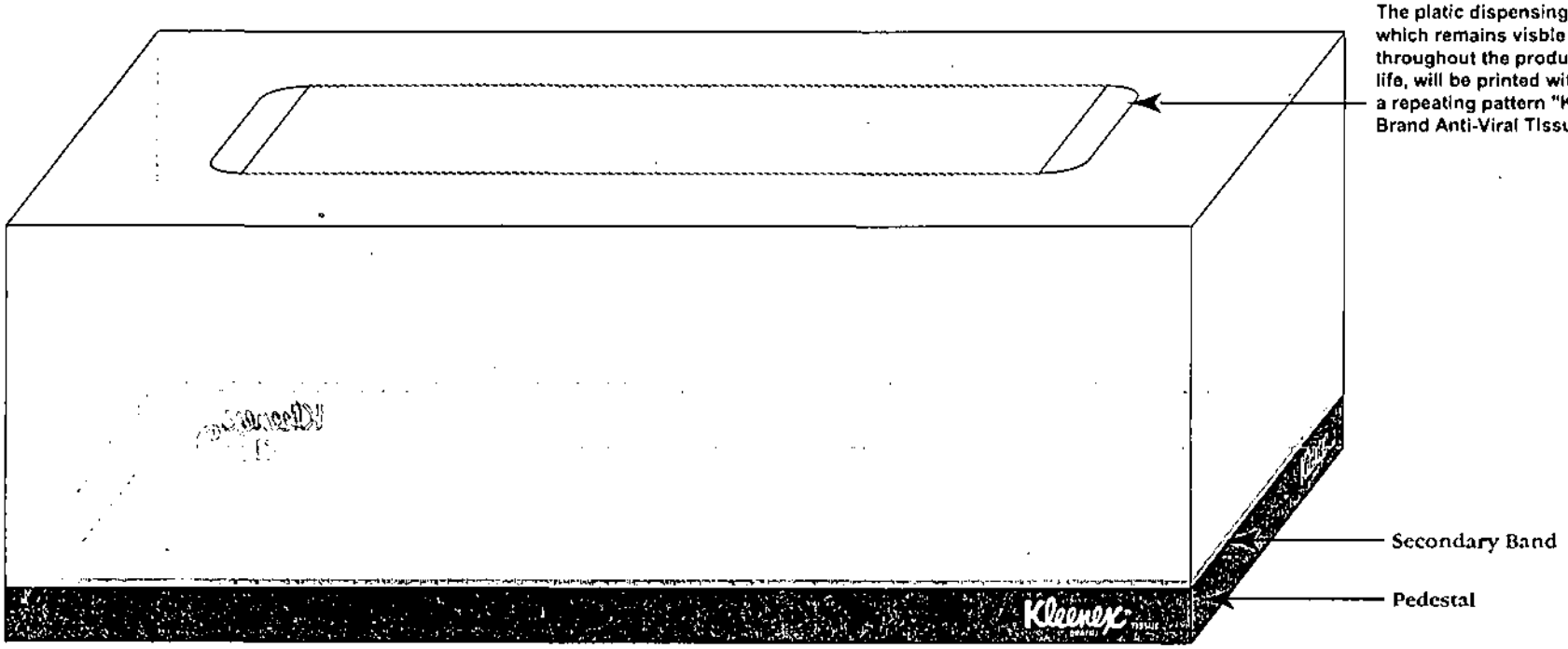
New!
Kleenex®
Anti-Viral™ BRAND TISSUE #2

Kleenex® BRAND TISSUE

Bottom Panel

76

NOT TO SCALE



77

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Kleenex® Anti-Viral BRAND TISSUE #2

LOOKING GLASS FOR POSITION ONLY UPC

Directions for Use: It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Use only as a facial tissue to help prevent the spread of cold and flu viruses†.

†**Virucidal Against:** Rhinoviruses Type 1A and 2 (Rhinoviruses are the leading cause of the common cold); Influenza A and Influenza B (causes of the flu); Respiratory Syncytial Virus (RSV–the leading cause of lower respiratory infection in children).

Storage and Disposal: Store in a dry area. Dispose of used tissues promptly. Do not reuse empty container.

1-800-553-3639 weekdays 8 a.m. to 4 p.m. CT

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Dept. XX-XX, PO Box 2020, Neenah, WI 54957-2020
Printed in USA.
Made in the USA from domestic and imported material.

www.kleenex.com

Made under the following U.S patents:
6,221,211; 5,227,242; 4,828,912; 4,738,847.

This box is made from 100% recycled paper.

EPA Reg. No.: XXXX-XXX
EPA Est. No.: XXXXX-XX-XX

ACTIVE INGREDIENTS:
Citric Acid 7.53%
Sodium Lauryl Sulfate 2.02%
INERT INGREDIENTS 90.45%
Total 100.00%

[120] 3-PLY TISSUES

78

07.30.03

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

August 14, 2003

SUBJECT: PRODUCT CHEMISTRY REVIEW OF: Kleenex Brand Anti-Viral Tissue #2

DP Barcode: D291513 **Reg. No. Or File Symbol: 9402-RN**
Manufacturing-use [ ] OR **End-use Product [X]**

: Adam Heyward PM 34 / Drusilla Copeland, Team Reviewer
Regulatory Management Branch II
Antimicrobials Division (7510C)

FROM: Robert A. Turpin, Chemist
Product Science Branch, CT Team
Antimicrobials Division (7510C)

THRU: Karen P. Hicks, CT Team Leader
Product Science Branch
Antimicrobials Division (7510C)

THRU: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Product Formulation

Active Ingredient(s)	**% by wt.**
Citric acid	7.51
Sodium lauryl sulfate	2.02

BACKGROUND: The applicant has submitted a revised Confidential Statement of Formula and a description of the formulation and manufacturing process of its product.

19

FINDINGS:

1. The Confidential Statement of Formula of the subject product dated June 24, 2003, is acceptable to the Agency. The extended certified limits of the active ingredient, citric acid, are acceptable in view of the process of formulation. The inert ingredients have been approved for use in pesticide products.

2. The descriptions of formulation and virucidal coating solution manufacturing are acceptable.

RECOMMENDATIONS: None.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

July 31, 2003

SUBJECT: PRODUCT CHEMISTRY REVIEW OF: Kleenex Brand Anti-Viral Tissue #2

DP Barcode: D292395 **Reg. No. Or File Symbol: 9402-RN**
Manufacturing-use [ ] OR **End-use Product [X]**

O: Adam Heyward PM 34 / Drusilla Copeland, Team Reviewer
Regulatory Management Branch II
Antimicrobials Division (7510C)

FROM: Robert A. Turpin, Chemist R. T.
Product Science Branch, CT Team
Antimicrobials Division (7510C)

THRU: Karen P. Hicks, CT Team Leader
Product Science Branch
Antimicrobials Division (7510C)

7/31/03

THRU: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Product Formulation

Active Ingredient(s)	**% by wt.**
Citric acid	7.51
Sodium lauryl sulfate	2.02

BACKGROUND: The applicant has, in response to a request from the Agency, submitted a study (MRID #460219-01) reporting the data requirements of 830.1650.

81

FINDINGS:

The description of the formulation process and application of the anti-viral coating to the tissue substrate of the subject product is acceptable to the Agency.

RECOMMENDATIONS: None.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

July 25, 2003

MEMORANDUM:

Subject: Efficacy Review EPA Reg.No. 9402-RN *Kleenex Brand Anti-Viral Tissue #2*
DP Barcode 289868 and DP Barcode 289966
Case No.072433

From: Nancy Whyte, Microbiologist NW
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

To: Adam Heyward/Drusilla Copeland
Regulatory Management Branch II
Antimicrobials Division (7510C)

Thru: Emily Mitchell, M.S., Team Leader Emily Mitchell 7/24/03
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

Thru: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Applicant: Kimberly-Clark Global Sales, Inc.
P. O. Box 2020
Neenah, WI 54957-2020

Formulation Label:

Active Ingredient(s)	%/wt
Citric Acid	7.51%
Sodium lauryl sulfate	2.02%
Other ingredients	90.47%
Total	100.00%

I. Background:

The registrant has submitted an application for a new product registration for a 3-ply tissue which makes claims that the tissue has antiviral properties against Rhinovirus

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Types 1A and 2 and Influenza A Virus and B Virus and Respiratory Syncytial Virus. The tissue makes no claims for antimicrobial action against bacteria or fungi. Two separate versions of the label were submitted--one with the package and a revised label with a disclaimer submitted after a meeting with representatives of the Agency. An additional updated label has been submitted since the revision was reviewed but was not available to this reviewer. This review encompasses two submissions, DP289868 and DP289966, which address issues raised in a pre-registration meeting with the Agency and Kimberly-Clark representatives.

The first package, D289868, contains a cover letter and a revised label. The second package, D289966, contains three articles which support the registrant's rationale for label claims of the product's effectiveness against four viruses known to be implicated in upper respiratory infections. The studies submitted were not conducted using Good Laboratory Practices. The first, MRID No. 459193-01, is a reprint of an article appearing in the *Journal of Infectious Diseases, Vol. 153, No. 2, February 1986,* which reports the results of a study of the interruption of the transmission of rhinovirus colds among human volunteers using virucidal paper handkerchiefs. The second document, MRID No.459193-02, is an article reprint from the same journal (*Vol. 152, August 1985)* which reports on the effect of placebo and virucidal paper handkerchiefs on viral contamination of the hand and transmission of experimental rhinoviral infection. The third document, MRID No. 459193-03, is a private communication which reports the results of virucidal screening studies that were conducted using lotion coating and silicone coating in the outer plies of the tissue to demonstrate complete inactivation of the organisms tested. Five viruses were used in this study--*Rhinovirus 1A, Rhinovirus 2, Influenza Virus A* and *Influenza Virus B,* and *Respiratory Syncytial Virus* . Also included in this document is a table which reports results of several studies conducted in June 2000, January and April 2001, and January 2002. The table lists the results of complete inactivation of the residual viruses by the tissues at various exposure periods when tissues containing either lotion or silicone are used as coatings in the presence of various concentrations of sodium lauryl sulfate and citric acid. This study was conducted by Kimberly-Clark and was reported in April 2003.

II. Use Directions:

There are no specific use directions printed on the box except that "this product is not to be used in a manner inconsistent with its labeling. Use only as a facial tissue to help prevent the spread of colds and flu viruses. "

III. Labeling:

1. There are several statements on the overwrap label attached to the box. The largest font type is used to describe the product (**The soft tissue now kills cold and flu viruses***). The next smaller font is used for an expanded claim for the value of the use of the product. A revised label has elevated the requested Agency claim disclaimer. which states that the product had not been tested against bacteria, fungi, and other viruses to the product description where it is more likely to be seen by consumers.

IV. Recommendations and Comments:

1. This product has limited use, and no other organisms other those presently approved may be added to the label claims for effectiveness of the product to control the transmission of cold and flu viruses without Agency review and approval.

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460219-00

LEWIS & HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

June 19, 2003

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RE
Applicant: Kimberly-Clark Corporation
Registration Application for New Product
Additional Information on the Formulation Process

Dear Adam:

On behalf of Kimberly-Clark Corporation, I am submitting three (3) copies of the following study. This information was requested by the review chemist, Robert Turpin:

- Volume 1 of 1
  Kleenex® Brand Anti-Viral Tissue #2: Process for Coating Add On; Formulation Process for Virucidal Coating Solution
  MRID# 46021901

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

85

LEWIS & HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

June 19, 2003

BY HAND

Jack E. Housenger
Associate Director, Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
Crystal Mall Building 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Re: Kleenex® Brand Anti-Viral Tissue #2, EPA File Symbol No. 9402-RE

Dear Jack:

We appreciate the time that you and your colleagues took to meet with Kimberly-Clark Corporation representatives on June 11, 2003 regarding Kimberly-Clark's pending application to register an antiviral facial tissue. This letter responds to the key questions and comments raised by EPA at our meeting and supplements our prior discussion of these issues in our February 26, 2003 and April 25, 2003 letters.

Virus Survival. In the course of our discussion of the 15-minute period required to achieve complete inactivation of residual viruses, you asked how long the targeted viruses survive on untreated tissues. The survival times of viruses have been well documented in the literature and can be summarized as follows for porous materials such as facial tissue. Copies of the cited references are being sent directly to Adam Heyward, the Product Manager for the Kleenex Brand Anti-Viral Tissue.

- Influenza: In the case of Influenza A, viral survival during storage was similar for cotton sheeting, serge, and dust. There was little loss of viability in 3 days; even after one week the loss of infectivity was slightly less than 2 logs (90%). It took two weeks for inactivation to reach 99%.

- Rhinovirus: Rhinovirus has been recovered after 3 hours from nonporous surfaces such as Formica and stainless steel. The virus survives well on some hard synthetic surfaces, such as nylon and Dacron, but were not isolated at times greater than 3 hours from porous fabrics such as facial tissue and cotton cloth.

- Respiratory Syncytial Virus: RSV survives from 30 minutes to 1 hour on paper and skin; however, it will survive up to 7 hours on counter tops, which would suggest that RSV may survive long enough on contaminated environmental surfaces to allow transfer of infective virus from surfaces to hands and from hands to susceptible mucosal sites of entry.

Table 1. Reported Survival Times of Viruses on Fomites [1]

Virus	Viral source	Fomite	Survival Time	Conditions
Influenza A strain PR8 [2]	Infected mouse lung suspension	Cotton sheeting, serge, dust	≥ 3 days	Ambient temperature and relative humidity, dark
			10% viable after 7 days	
			1% viable after 2 weeks	
		Glass slides	10% viable after 3 days	Ambient temperature and relative humidity, dark
			0.01% viable after 5 weeks	
Rhinovirus [3]	Nasal mucus	Plastic	≤24 hr	23°C, ambient relative humidity
	Cell culture virus in Hanks balanced salt solution (BSS)	Plastic	≤24 hr	23°C, ambient relative humidity
	Cell culture virus in Hanks BSS or 0.85% NaCl	Formica, stainless steel, varnished wood, hard synthetic fabrics, wool, silk	>3 hr	23°C, ambient relative humidity
		Cotton, rayon, paper, towel, facial tissue	>1 but <3 hr	23°C, ambient relative humidity
Respiratory syncytial virus [4]	Infected cell culture or nasal secretions	Counter tops	7 hr	Composition of surface more important than variations in temperature, relative humidity, or drying time
		Gloves	2-5 hr	
		Cloth	2 hr	
		Paper and skin	30-60 min	

[1] Gerba, Charles P. and Goyal, Sagar M., Methods in Environmental Virology, Marcel Dekker, Inc., 1982, pages 184-185, 190-192, 202-203.

[2] Edwards, D.G., Resistance of influenza virus to drying and its demonstration on dust, Lancet 241:664-666.

[3] Hendley, J.O., Wenzel, R.P., and Gwaltney, J.N. Jr., Transmission of rhinovirus colds by self-inoculation, New England Journal of Medicine, 1973, 288:1361-1364.

[4] Hall, C.B., Douglas, R.G. Jr., and Geiman, J.M., Possible transmission by fomites of respiratory syncytial virus, Journal of Infectious Disease, 1980, 141:98-102.

Thus, even if no viruses were killed for a full 15 minutes, viral survival on the tissues would still be substantially reduced compared to an untreated tissue, with a corresponding reduction in the opportunities for the viruses to be transmitted to others. In fact, of course, the effect of the treated tissues is even more significant because, as shown by the data submitted with our April 25 letter and discussed at our meeting, the great majority of the viruses are killed within the first couple of minutes. As discussed, given the enormous health, economic, and social costs of colds and flus, even a modest percentage reduction in their transmission would be of significant benefit. (We refer you to our April 25 letter for a more detailed discussion of the product's benefits notwithstanding the 15-minute time for inactivation of residual viruses.)

Label Language. EPA also asked Kimberly-Clark to consider additional label language to further EPA's objective of better educating consumers regarding the spread of colds and flu viruses and the tissue's role in helping to limit the transmission of such viruses. In response to that request, Kimberly-Clark has revised its label; the new proposed label is enclosed. In addition to explaining the role of the tissue in helping to limit the spread of cold and flu viruses by hand contact, the label specifically notes that the product has not been tested against bacteria and fungi. We believe the new label addresses EPA's concerns and makes it clear what can – and can not – be expected from the product.

Disinfectant Standard. At our meeting, we also continued the discussion between Kimberly-Clark and EPA with respect to whether the antiviral tissue, in the absence of bactericidal data, should be registered. While Kimberly-Clark recognizes the Agency's concern about registering products that have not been tested against representative bacteria, we believe that there are special circumstances that should lead the Agency to waive such data. Regarding the antiviral tissue, we believe that bacterial data are not pertinent and would not provide any useful information. Moreover, establishing a "hard rule" that would preclude the registration of targeted or niche products, such as the antiviral tissue, will prevent the introduction of products that clearly have important public health benefits.

Elaborating on the discussion in our April 25 letter, the following points should also be noted.

- There is currently no legal or regulatory requirement that virucides show sufficient bactericidal efficacy to meet disinfectant standards.

- EPA's 1999 proposed antimicrobial regulations and its draft antimicrobial data requirements would impose disinfectant efficacy standards on a variety of products, but neither set of regulations has been promulgated as final. Even if the regulations were final, however, they provide sufficient flexibility that EPA could register the Kimberly-Clark tissue without requiring antibacterial efficacy data. For example, the proposed antimicrobial regulations contain a "virucide only" category for products used on hard surfaces, thereby recognizing that it is possible, with appropriate limitations on product claims,

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for a registered virucide not to be a broad spectrum disinfectant. *See* proposed 40 C.F.R. 156.446(b)(2), 64 *Fed. Reg.* 50672, 50723 (Sept. 17, 1999). The draft data requirements specify studies for products with combined disinfectant and virucidal claims, but not for products like the tissue that make only virucidal claims, leaving the Agency with the latitude to tailor efficacy requirements to the specific, limited claims being made. And, of course, even if there were a binding general requirement for all virucides to demonstrate antibacterial efficacy, EPA's regulations recognize the necessarily case-by-case nature of data requirements and the Agency's discretion to waive inappropriate data requirements. *See* 40 C.F.R. §§ 158.25(b), 158.35, and 158.45.

- As we have discussed, Kimberly-Clark's previous antiviral tissue, registered under the same regulations in effect today, was approved without antibacterial efficacy data. Indeed, we can find no record that EPA suggested that such data were appropriate.

- We understand that EPA's proposal to require disinfectant-level efficacy data on various products for which disinfectant claims were not explicitly made was an effort to prevent consumers from being misled by broad, generalized antimicrobial claims. EPA has, in effect, proposed to require that claims likely to be understood as antibacterial be supported by antibacterial efficacy data. However, that concern is inappropriate in this case. Kimberly-Clark is not making a generalized antimicrobial claim. The product claims are limited to preventing the transmission of cold and flu viruses and – especially with the additional label language discussed above – can not reasonably be understood[1] as antibacterial claims for which disinfectant level efficacy should be established.

Other Issues. As discussed at our meeting and in our prior correspondence, we do not believe that there are other issues requiring resolution in order for EPA to register the antiviral tissue. Specifically, we have addressed the Agency's questions with respect to the organic soil loadings in the efficacy testing of the tissue; based on our discussion at the meeting, we believe the coding of the remaining inerts is being addressed; and we do not believe that there are toxicity issues with respect to the product.

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[1] It is not possible, of course, to guard against every conceivable misunderstanding, no matter how unreasonable. However, pesticide labeling is the cornerstone of FIFRA's regulation of pesticides. FIFRA thus assumes that label language – including qualifications, and limitations – is meaningful and can be tailored to the particular characteristics of a product. EPA should not overturn that fundamental premise by, in essence, taking the position that limitations and explanations of a product's claims, no matter how clear, are meaningless and must therefore be read as encompassing broader claims that, in turn, trigger broader data requirements.

Timing. Finally, as we described, the lead time to obtain state registrations; have the necessary production equipment manufactured, tested, and installed; and manufacture sufficient product to introduce the antiviral tissue by August 2004 is extensive. Kimberly-Clark's management does not believe that it can responsibly make the significant capital investment necessary to launch the product until it has the assurance (in the form of EPA and state registrations) that it will be able to market the product on a national basis. Accordingly, we respectfully request that EPA make a decision on Kimberly-Clark's registration application by July 15, 2003.

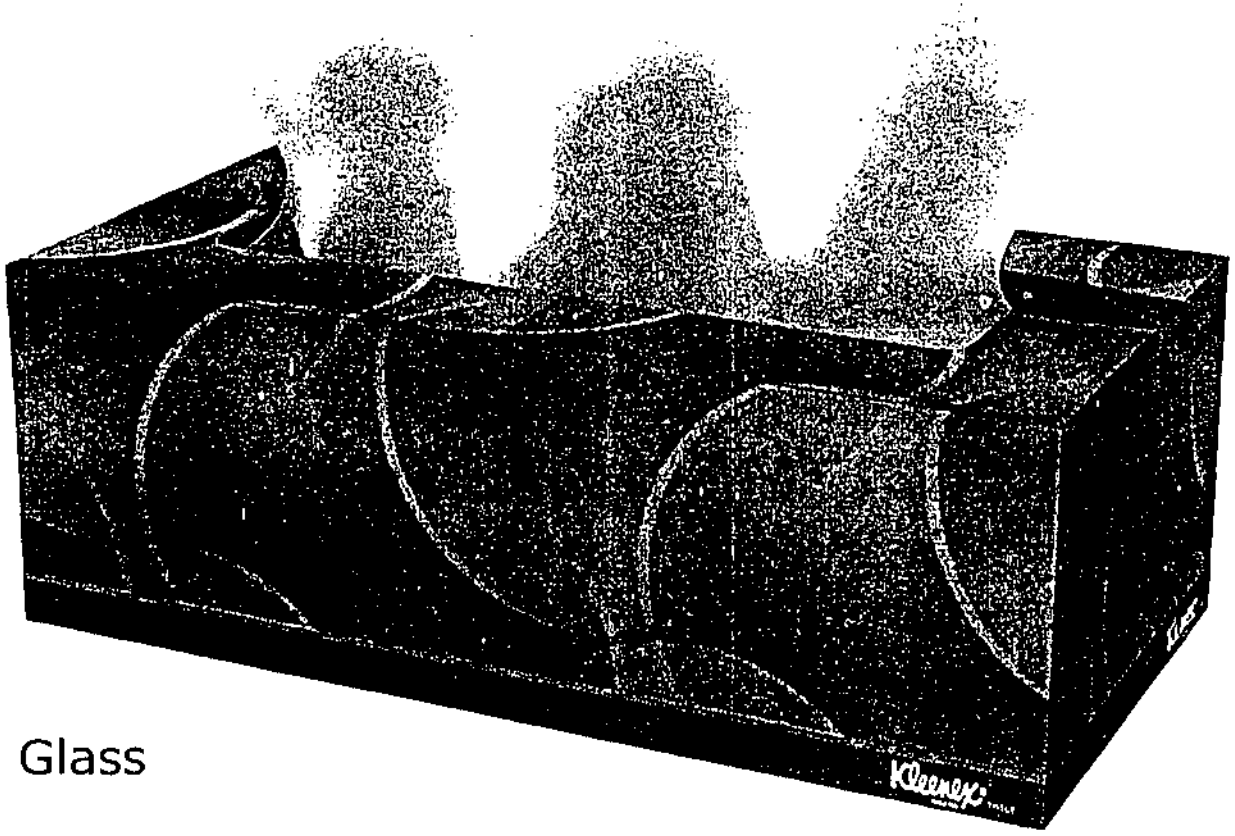
Thank you for your time and consideration.

Sincerely,

Eliot I. Harrison, Agent for
Kimberly-Clark

cc: Connie Welch, Branch Chief, Regulatory Mgmt. Br. No. 2

90



Looking Glass

Facial Tissue Product with Overwrap

ACTIVE INGREDIENTS:
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Sodium Lauryl Sulfate 2.02%
INERT INGREDIENTS 90.45%
Total 100.00%

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120 3-PLY TISSUES • 8.6 x 8.4 in / 21.8 x 21.3 cm

Principal Display Panel

New!
Kleenex®
Anti-Viral™ BRAND TISSUE

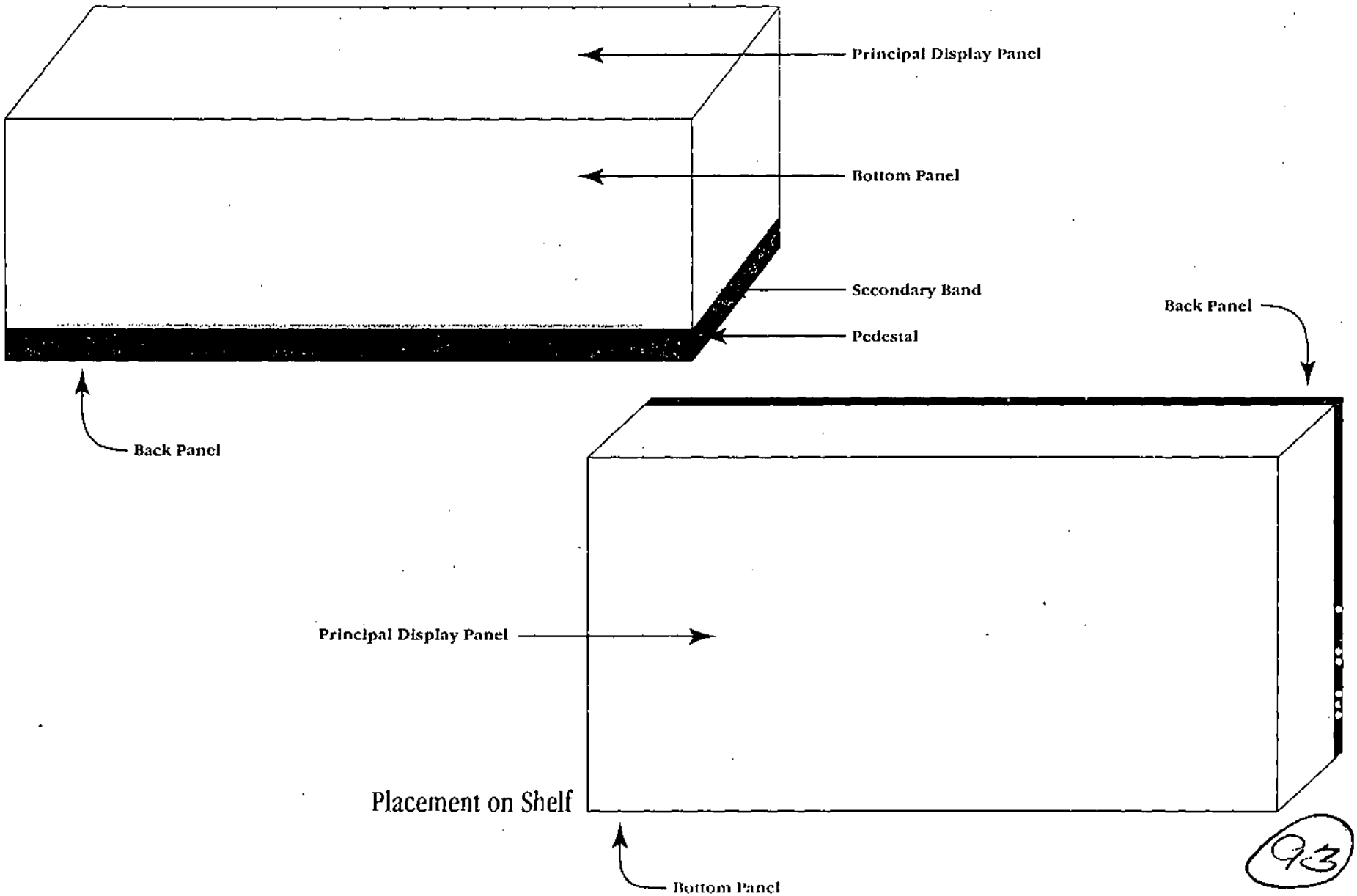
Kleenex® BRAND TISSUE

Bottom Panel

92

Facial Tissue Product with Overwrap – Overall View

NOT TO SCALE



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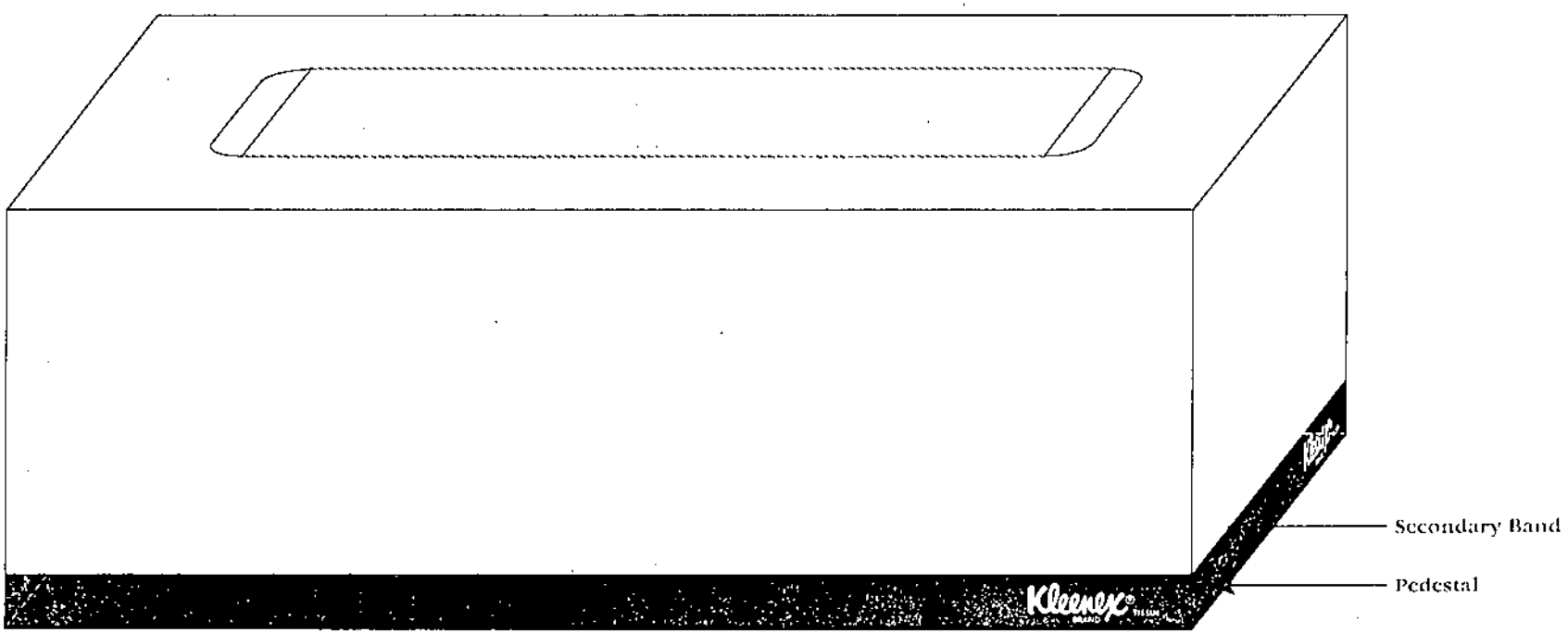

94

459193-(

LEWIS & HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

April 25, 2003

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RA
Applicant: Kimberly-Clark Corporation
Registration Application for New Product
Data Transmittal Letter for Efficacy Studies being Submitted as a Follow-Up to April 9, 2003 Meeting

Dear Adam:

As a follow-up to the April 9, 2003 meeting between representatives from Kimberly-Clark and Agency staff, I am submitting, on behalf of Kimberly-Clark, three (3) copies of the following studies:

- Volume 1 of 3
  Interruption of Transmission of Rhinovirus Colds Among Human Volunteers Using Virucidal Paper Handkerchiefs
  MRID# 45919301
- Volume 2 of 3
  The Effect of Placebo and Virucidal Paper Handkerchiefs on Viral Contamination of the Hand and Transmission of Experimental Rhinovirus Infection
  MRID# 45919302

(95)

- Volume 3 of 3
  Summary of Time-Kill Studies Conducted with Anti-Viral Tissue
  MRID# 45919303

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

C16

Note to reviewer: All text in brackets [xxx] is optional and may or may not be included on a final label.
All text in braces {xxx} is administrative and will not appear on a final label.
Final packaging may be translated into French and/or Spanish

{FRONT PANEL:}

{Primary Brand Name:} Kleenex® Brand Anti-Viral* Tissue #2

Net Contents: [1 through 150] 3-Ply [White] [Printed] Tissues 8.6x 8.4in / 21.8 x 21.3 cm

ACTIVE INGREDIENTS:
Citric Acid.....7.51%
Sodium Lauryl Sulfate.....2.02%
INERT INGREDIENTS:.....90.47%
Total:.....100.0%

Kleenex® Brand [Tissue]

Open Here

[Date code]

97

Note to reviewer: All text in brackets [xxx] is optional and may or may not be included on a final label.
All text in braces {xxx} is administrative and will not appear on a final label.
Final packaging may be translated into French and/or Spanish

{FRONT OR BACK PANEL MARKETING CLAIMS:}

[New] {*"New" will only appear on the label for the first 6 months of distribution*}

[New] [Try-Me] [NOW] [Anti-Viral* Tissue!] [NOW with] [Anti-Viral* Formula!] [Virus*-Neutralizing Formula] [Neutralizes Cold & Flu Viruses*] [Cold & Flu Germs*] [Viruses*!] [Cold & Flu Virus*] [Virus* Neutralizing Layer!] [Kills] [Neutralizes] [99.9% of] [Cold & Flu Germs*] [Cold & Flu Viruses*] [Viruses*] [See back panel for details] [Still just as] [soft]

[Stop Spreading Cold & Flu Germs*] [Anti-Viral* Ingredients]

[Prepare for [Cold & Flu Viruses*] [Viruses*] [Cold & Flu Germs*]]

[Help Stop the Cold & Flu [Virus*] Cycle]

[Help stop the Cycle of Cold & Flu [Viruses*]]

[Help Stop the Spread of [Cold & Flu Germs**] [Cold & Flu Viruses*] [Viruses*]]

[Introducing a revolution in facial tissues!]

[Keep [Cold & Flu] [Viruses*] [Germs*] to Yourself]

[It's Cold & Flu Season – Be Prepared!]

[Now You Can Prepare for Cold & Flu Season]

[Ready for Cold & Flu Season?]

[Help Break the Cycle of] [Cold & Flu Germs*] [Viruses*] [Cold & Flu Viruses*]

[Help Keep [Cold & Flu Viruses*] [Viruses*] [Cold & Flu Germs*] From Spreading]

[KLEENEX® tissue – a barrier of protection against everyday] [cold & flu germs*] [cold & flu viruses*] [viruses*]]

[Block] [Cold [& Flu] Germs*] [Cold [& Flu] Viruses*] [Viruses*]

[New] [KLEENEX® [Ultra Soft] ANTI-VIRAL* Tissues have [GermBlocker*] [Anti-Viral* Blue Layer] [Cold [&Flu] Virus* Lock] [Cold & Flu][Germ Barrier*] [Germ Defense*] [Germ Shield*] a new middle layer [formula] that's [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [viruses*] [germs*] [cold & flu viruses*] [cold & flu germs*] that cause colds and flu. Be prepared with [soft], [three-layered] KLEENEX® ANTI-VIRAL* Tissues.]

[Now KLEENEX® [Ultra Soft] Tissue gives you [a] [an] [super soft] [soft], anti-viral* tissue with a special [moisture activated] middle layer [formula] [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [cold & flu viruses*] [viruses*] [cold & flu germs*.]] [Help Stop the cycle of [cold & flu viruses*] [viruses*] [cold & flu germs*] in your family.] [Try new KLEENEX® [Ultra Soft] ANTI-VIRAL* Tissues today.]

[We're always looking for ways to help keep your family happy. That's why [soft], [new] KLEENEX® [Ultra Soft] ANTI-VIRAL* Tissues have a special middle layer [formula] that's [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [cold & flu germs*] [viruses*] [cold & flu viruses*]. [Buy them for your family this season.]]

[[Scientifically] [Clinically] proven, [New] Kleenex® [Ultra Soft] Anti-Viral* Tissues [neutralize] [kill] [99.9% of] [cold & flu viruses*] [viruses*] [cold & flu germs*].] [Use [new] [super soft] Kleenex® [Ultra Soft] Anti-Viral* tissues to help stop the cycle of [cold & flu germs*] [cold & flu viruses*] [viruses*] in your home.]

[Only KLEENEX® [Ultra Soft] Tissue gives you a tissue with [three] [super soft] [soft] layers, including a middle layer [formula] [scientifically] [clinically] [proven] [to] [that] [neutralize] [kill] [99.9% of] [viruses*] [cold & flu viruses*] [cold & flu germs*].]

[New] [KLEENEX® [Ultra Soft] Anti-Viral* Tissues have a unique [moisture activated] middle layer [formula] [scientifically] [clinically] proven to [neutralize] [kills] [common] [viruses*] [germs*] that cause colds & flu.]

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Note to reviewer: All text in brackets [xxx] is optional and may or may not be included on a final label.
All text in braces {xxx} is administrative and will not appear on a final label.
Final packaging may be translated into French and/or Spanish

[New] [KLEENEX® [Ultra Soft] Anti-Viral* Tissues have three [soft] layers and a special moisture-activated formula [middle layer] that [is] [clinically] [scientifically] [proven to] helps stop the spread of [cold & flu viruses*] [viruses*] [cold & flu germs*].]

[New] [KLEENEX® [Ultra Soft] Anti-Viral* Tissues help stop the spread of [cold & flu germs*] [cold & flu viruses*] [viruses*]. These new tissues have a unique [moisture activated] special middle layer [formula] that [is] [clinically] [scientifically] [proven to] [neutralizes] [kills] [99.9% of] [common] [viruses*] [germs*] that cause colds and flu.]

[New] [KLEENEX® [Ultra Soft] Anti-Viral* Tissues have a moisture-activated middle layer [formula] that [stops] [neutralizes] [kills] most [common] [cold & flu viruses*] [viruses*] [cold & flu germs*].]

[For noses [that just want] extra comfort, now [our] [the] [softest] tissues, Kleenex® [Ultra Soft] Brand Tissues, have Anti-Viral* protection.] [[Scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [cold & flu germs*] [cold & flu viruses*] [viruses*].]

[Our] [the] [softest] [three-layered] Kleenex® [Ultra Soft] Brand Tissues now have Anti-Viral* protection! With a [special] [unique] [moisture activated] middle layer [formula] that is [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [cold & flu germs*] [cold & flu viruses*] [viruses*].]

[Now [our] [the] [softest] [three layered] Kleenex® [Ultra Soft] Brand Tissues gives you an Anti-Viral* middle layer [formula] [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [viruses*] [cold & flu viruses*] [cold & flu germs*]. Help stop the cycle of [cold & flu viruses*] [viruses*] [cold & flu germs*] in your family. Try [new] KLEENEX® [Ultra Soft] ANTI-VIRAL* Tissues today.]

[It seems that once one person in the family gets a cold it's only a matter of time before everyone else gets it.] [Introducing new KLEENEX® Anti-Viral [revolutionary] tissues [with a treated middle layer] that kills 99.9% of cold and flu germs [in the tissue].]

[Especially designed for the whole family] [Great for use in hospitals, schools, churches, day care facilities, physicians' offices'.]

[Look for the blue dot pattern.]

[KLEENEX® Anti-Viral tissues with the blue dots.]

[*Thank Goodness for Kleenex® tissue.*]

{Alternate Brand Names:} Kleenex® [Ultra Soft] Brand [with] [Advanced Care] [Anti-Germ*] [Anti-Viral*] [GermBlock*] Tissue

{When final graphics are selected, the name of the graphic will appear above the UPC symbol. The name, while short, typically describes some element of the graphic so that consumers have a specific reference when contacting Kimberly-Clark via the Consumer Services Department.}

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Note to reviewer: All text in brackets [xxx] is optional and may or may not be included on a final label.
All text in braces {xxx} is administrative and will not appear on a final label.
Final packaging may be translated into French and/or Spanish

{*BACK PANEL:*}

Directions for Use: It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Use to help prevent the spread of [viruses*] [cold & flu viruses*] [cold & flu germs*]. [Complete] [Total] [99.9%][neutralization] [kill] [inactivation] of [target] viruses* within 15 minutes [after contact].

*Virucidal Against: Rhinoviruses Type 1A and 2 [Rhinoviruses are the leading cause of the common cold], Influenza A and Influenza B [cause of the flu], Respiratory Syncytial Virus [RSV – the leading cause of lower respiratory infection in children].

Storage and Disposal: Store in a dry area. Dispose of used tissues in a normal fashion. Do not reuse empty container.

1-800-553-3639 weekdays 8 a.m. to 4 p.m. CT
Kimberly-Clark Corporation, Dept. [XXX]-108
PO Box 2020, Neenah, WI 54957-2020

Printed in USA
Made in USA {graphic}

www.kleenex.com

Made under the following US patents: _____

{*Graphic*} This box is made from 100% recycled paper
{*UPC Symbol*}

EPA Registration No._____
EPA Est. No. _____

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Help Stop the Cycle of Cold & Flu

Now KLEENEX® Brand gives you a soft, anti-viral† tissue with a special moisture-activated middle layer scientifically proven to kill 99.9% of cold and flu viruses†. Help stop the cycle of cold and flu viruses in your family. Try new KLEENEX® Anti-Viral™ Tissues today.

Kleenex® Anti-Viral BRAND TISSUE

LOOKING GLASS FOR POSITION ONLY UPC

Directions for Use: It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Use only as a facial tissue to help prevent the spread of cold and flu viruses†. 99.9% neutralization of cold and flu viruses† in the tissue within 15 minutes.

†Virucidal Against: Rhinoviruses Type 1A and 2 (Rhinoviruses are the leading cause of the common cold); Influenza A and Influenza B (causes of the flu); Respiratory Syncytial Virus (RSV–the leading cause of lower respiratory infection in children).

Storage and Disposal: Store in a dry area. Dispose of used tissues in a normal fashion. Do not reuse empty container.

1-800-553-3639 weekdays 8 a.m. to 4 p.m. CT

Distributed by Kimberly-Clark Global Sales, Inc.,
Dept. XX-XX, PO Box 2020, Neenah, WI 54957-2020
Printed in USA.
Made in the USA from domestic and imported material

www.kleenex.com

Made under the following US patents:
6,221,211; 5,227,242; 4,828,912; 4,738,847.

This box is made from 100% recycled paper.

EPA Reg. No.: XXXX-XXX
EPA Est. No.: XXXXX-XX-XX

ACTIVE INGREDIENTS:
Citric Acid 7.53%
Sodium Lauryl Sulfate 2.02%
INERT INGREDIENTS 90.45%
Total 100.00%

120 3-PLY TISSUES

Original

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LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

April 25, 2003

BY HAND DELIVERY AND FACISIMILE

Mr. Adam Heyward, Product Manager (34)
Regulatory Management Branch #2
U.S. Environmental Protection Agency
Antimicrobial Division (7510C), Office of Pesticide Programs
1921 Jefferson Davis Highway, Crystal Mall #2, Room 308B
Arlington, VA 22202

Re: Kleenex ® Brand Anti-Viral Tissue #2
EPA File Symbol No. 9402-RE
April 9, 2003 EPA Meeting with Kimberly-Clark Corporation

Dear Adam:

Thank you and your colleagues for taking the time to meet on April 9, 2003 with representatives of Kimberly-Clark Corporation regarding the above-referenced registration application. This letter summarizes the discussion at the meeting concerning EPA's November 25, 2002 comments on the application and Kimberly-Clark's February 26, 2003 response, and encloses additional materials discussed at the meeting.

Product Efficacy and Benefits

The primary topic discussed was the efficacy and expected benefit of Kimberly-Clark's product, which, as you know, is a three-ply facial tissue, the center ply of which is treated with a virucidal coating containing citric acid and sodium lauryl sulfate as active ingredients. The virucidal coating has been shown to be effective against flu and cold viruses using methodology previously approved by the Agency, and Kimberly-Clark believes that the tissue will help prevent the spread of flu and cold viruses. EPA has raised three primary issues with respect to the product's effectiveness and benefits.

1. 15-Minute Inactivation Time. Our understanding is that EPA agrees that a tissue that inactivates cold and flu viruses would benefit public health. However, EPA questions whether the benefit of the Kimberly-Clark tissue would be meaningful in light of the 15-minute time period necessary to achieve the required 99.9% reduction of virus with complete inactivation of residual virus. EPA asserts that most tissues are discarded only a minute or two after use and that the product should achieve 99.9% inactivation in that time period. While we agree that, in an ideal world, such an outcome would be preferable, we believe that the efficacy level established by the studies supporting Kimberly-Clark's application are of significant potential benefit for the following reasons.

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- First, most of the viral reduction does, in fact, occur in the first couple of minutes. The full 15-minute period is necessary only to achieve the inactivation of residual viruses as required to satisfy the 99.9% reduction standard. As we discussed, trials conducted by Kimberly-Clark prior to the GLP efficacy studies submitted with the application demonstrated significant inactivation during the first two minutes. Copies of those studies are enclosed along with a summary of the data. Thus, we believe that cold and flu viruses are reduced to levels below infectious doses very quickly, providing significant benefits even if tissues are discarded after only a couple of minutes.

- Second, we know of no data supporting EPA's assertion that most tissues are discarded a minute or two after use. While such a practice is certainly preferable, there are many situations in which a person using a tissue does not have ready access to a waste can and retains the tissue in a pocket or purse until it can be discarded; in addition, some users (children, for example) may not be as sensitive as we would like to the desirability of promptly discarding used tissues. In fact, a Kimberly-Clark mall intercept study, submitted in support of its application, showed that approximately half of the people carrying tissues were carrying used tissues. Moreover, even discarded tissues may be handled when trash cans are emptied. Accordingly, even with a longer inactivation period, the tissue still offers a meaningful potential to reduce the spread of cold and flu viruses from the handling of used tissues.

- Increasing the level of active ingredients in the product to shorten the inactivation time could make the tissue irritating to sensitive skin, reducing the product's use and, thus, its benefits.

- Kimberly-Clark's proposed label claims, as reflected on the enclosed prototype label, make it clear that the complete inactivation of residual virus is reached only after 15 minutes, and that the product simply helps prevent the spread of viruses, rather than curing them. We do not believe that consumers will be misled about the extent of the product's benefits.

- Unlike other products (e.g., hard surface disinfectants) with longer inactivation times, the user's behavior cannot render the tissue ineffective. A user can wipe off a surface disinfectant prematurely, eliminating the product's benefit. In the case of the tissue, however, the virucide is an integral part of the product and will act on the viruses trapped in the tissue regardless of how the consumer handles the tissue after use.

- Kimberly-Clark does not expect or claim that the tissue will completely eliminate the spread of colds or flu viruses. However, studies conducted with Kimberly-Clark's previously registered virucidal tissue, Kleenex Avert Virucidal Tissue (Reg. No. 9402-3), demonstrated that the treated tissue concept is a sound one and that the Avert tissue did reduce the transmission of

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viruses. See the two enclosed articles from *The Journal of Infectious Diseases*. As we have discussed, the current tissue has a lower concentration of active ingredient to provide a tissue that is not irritating to the skin. However, given the efficacy data on the current product, Kimberly-Clark is confident that it, like its predecessor, can provide a real benefit in reducing the spread of cold and flu viruses.

- There is currently no comparable or alternative product available, so any reduction in the spread of viruses that the tissue achieves would represents a public health improvement over the status quo. The FDA estimates that flu is responsible for between 15 and 111 million lost workdays every year in addition to related medical costs.[1] Just this year, the Centers for Disease Control released data increasing CDC's estimate of the number of annual deaths attributable to flu and RSV from 20,000 to 36,000.[2] According to "Management of the Common Cold;" *Adv. Intern Med* 32:207-234, (1987), "Sniffles, common colds and other upper respiratory infections are the most frequent acute illnesses in the United States and throughout the industrialized world. In 1982, according to the National Health Interview Study, [which reported only colds that lead to medical attention or at least one day of restricted activity] 380 million episodes of acute illness and injury from all causes occurred among the civilian population of the United States; 71 million (19%) were common colds." Given the significant mortality, time and productivity losses, discomfort, and expense associated with widespread colds and flu, even a modest percentage reduction in new cases of colds or flu would be a meaningful benefit. In light of the absence of risk concerns regarding the tissue, which contains only "minimum risk" active ingredients and which EPA has placed in Toxicity Category IV, the FIFRA risk-benefit standard for registration is easily satisfied.

2. Disinfectant Standards. EPA has suggested that, regardless of effectiveness against targeted viruses, the Agency cannot accept a "virucide" claim for the product unless it also satisfies the antibacterial criteria for qualifying as a disinfectant. We believe that such a requirement is wholly inappropriate for this product.

- As reflected on the enclosed label, Kimberly-Clark makes no antibacterial claims for the product. Claims are limited to cold and flu viruses, and the tissue's efficacy against the targeted viruses has been demonstrated. No

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[1] FDA, "How to Avoid the Flu," *FDA Consumer Magazine* (Nov. 1994) (reprint available at www.fda.gov/fdac/reprints/flu.html)

[2] www.cdc.gov/od/oc/media/pressrel/r030107.htm

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purpose would be served by requiring Kimberly-Clark to prove efficacy against organisms not intended to be controlled by the product.

- There is no legal requirement that antibacterial efficacy be shown to support a virucide registration. We recognize that EPA has proposed such a regulation, but that regulation has not been promulgated; even if it had been, EPA would still retain its authority to waive data requirements inappropriate for the product and label under consideration.

- Under the regulations and guidelines that remain in effect today, Kimberly-Clark's very similar predecessor product; Kleenex Avert Virucidal Tissue, was registered by EPA with exclusively virucidal claims and without being required to demonstrate disinfectant-level control of bacteria.

- The Antimicrobial Division has placed great emphasis in recent years on curbing antimicrobial claims that, even if technically accurate, are irrelevant or create a misimpression among consumers about the benefits or effects of a product. Here, the focus is on nasal secretions associated with colds and flu, where the organisms of public health relevance are viruses rather than bacteria. Antibacterial claims are irrelevant to this product, would serve only to confuse users and will not appear on the product label, and there is no need or requirement to verify the accuracy of nonexistent claims.

3. Soil Loading. EPA has also questioned whether the organic soil loadings during efficacy testing of the tissue were sufficient to evaluate effectiveness against the target viruses in the presence of mucous and other discharges. As discussed during our meeting, and in the references provided to Nancy Whyte at the meeting (which were also included with our February 26, 2003 response), there is available information on the level of soil loading that can reasonably be expected from use of this product. The soil loadings at which the tissue's efficacy were tested equal or exceed those expected levels. If higher organic soil loadings were to be used, the ability of the testing to evaluate the product's efficacy could be impaired as the protein soil could cause rapid growth and death of the host cells. Death of the host cells would impair the virologist's ability to determine the presence of active virus. Accordingly, Kimberly-Clark believes that the organic soil loadings used in its efficacy testing were appropriate for ensuring an accurate evaluation of the product's effectiveness and in line with, or greater than, the soil loads that would be seen in actual product use based upon data derived from government health agencies.

Product Chemistry

As discussed, Kimberly-Clark believes that it has fully addressed the product chemistry issues identified in EPA's November 25 letter and that the necessary information for clearance of the remaining inert ingredients has been provided to the Agency. We requested that you confirm that there are no outstanding product chemistry issues or questions.

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Toxicology

We also believe that there are no outstanding toxicology concerns. We agree with the Category IV classification of the product. Our February 26 submission did include the results of some human studies such as are routinely conducted by Kimberly-Clark and other consumer product companies to ensure the safety of their products. The studies showed some incidence of moderate and reversible dermal irritation in a scenario reflecting significant and prolonged product misuse, but confirmed that the tissue is not an irritant under normal use or other misuse conditions. Although, out of an abundance of caution, the study was submitted under Section 6(a)(2), we do not believe that it affects the terms of the requested registration or the results of the previous EPA toxicology review.

Timing

In order to launch this product on a timely basis, it is important to Kimberly-Clark that any remaining issues be resolved promptly so that the EPA registration can be issued in time for Kimberly-Clark to obtain the necessary state registrations prior to marketing the product. We would therefore appreciate EPA's response on any outstanding issues at your earliest convenience.

Thank you for your time and attention.

Sincerely,

Eliot I. Harrison,
Agent for Kimberly-Clark

Enclosures

cc: Connie Welch, Branch Chief
Michael Caringello, Kimberly-Clark Corporation
Cynthia Lewis, Beveridge & Diamond, P.C.

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459193-0

LEWIS & HARRISON
Consultants In Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
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April 25, 2003

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RE
Applicant: Kimberly-Clark Corporation
Registration Application for New Product
Data Transmittal Letter for Efficacy Studies being Submitted as a Follow-Up to April 9, 2003 Meeting

Dear Adam:

As a follow-up to the April 9, 2003 meeting between representatives from Kimberly-Clark and Agency staff, I am submitting, on behalf of Kimberly-Clark, three (3) copies of the following studies:

- Volume 1 of 3
  Interruption of Transmission of Rhinovirus Colds Among Human Volunteers Using Virucidal Paper Handkerchiefs
  MRID# 45919301
- Volume 2 of 3
  The Effect of Placebo and Virucidal Paper Handkerchiefs on Viral Contamination of the Hand and Transmission of Experimental Rhinovirus Infection
  MRID# 45919302

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- Volume 3 of 3
  Summary of Time-Kill Studies Conducted with Anti-Viral Tissue
  MRID# 45919303

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

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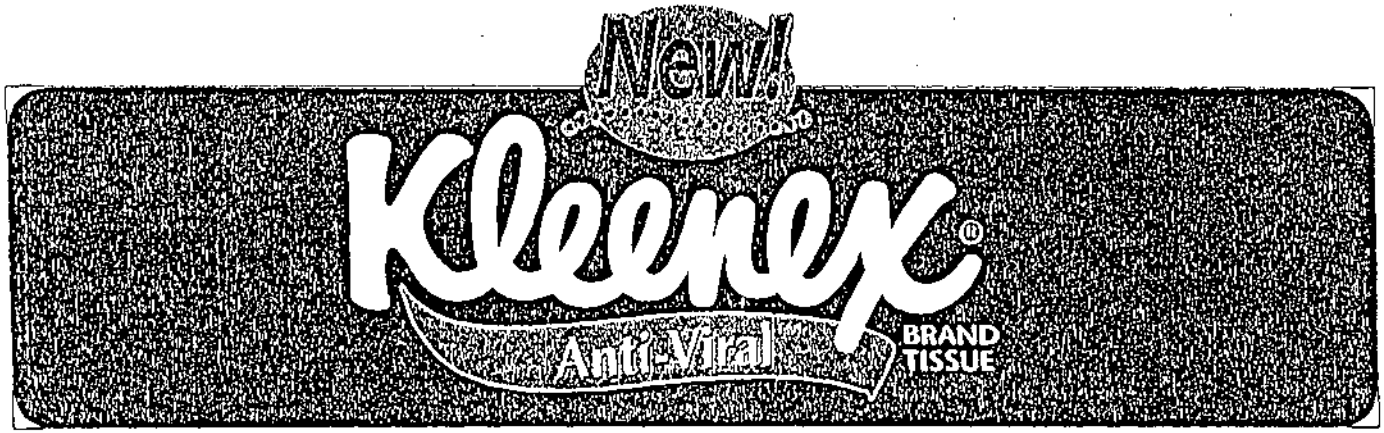
ACTIVE INGREDIENTS:
Citric Acid 7.53%
Sodium Lauryl Sulfate 2.02%
INERT INGREDIENTS 90.45%
Total 100.00%

Facial Tissue Product with Overwrap

Principal Display Panel

120 3-PLY TISSUES • 8.6 x 8.4 in / 21.8 x 21.3 cm



Bottom Panel

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Revised June

Help Stop the Cycle of Cold & Flu

A leading cause of the spread of cold and flu viruses is by hand contact. With regular tissues, cold and flu viruses can be transferred from the tissue to your hands, surfaces, and other objects, and then be retransmitted to others. Now KLEENEX® Brand gives you a soft, anti-viral† tissue with a special moisture-activated middle layer scientifically proven to kill 99.9% of cold and flu viruses† in the tissue within 15 minutes. Help stop the cycle of cold and flu viruses in your family. Try new KLEENEX® Anti-Viral™ Tissues today.

Kleenex® Anti-Viral BRAND TISSUE

LOOKING GLASS

FOR POSITION ONLY

UPC

Directions for Use: It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Use only as a facial tissue to help prevent the spread of cold and flu viruses†.

†Virucidal Against: Rhinoviruses Type 1A and 2 (Rhinoviruses are the leading cause of the common cold); Influenza A and Influenza B (causes of the flu); Respiratory Syncytial Virus (RSV–the leading cause of lower respiratory infection in children). This product has not been tested against bacteria and fungi.

Storage and Disposal: Store in a dry area. Dispose of used tissues promptly. Do not reuse empty container.

1-800-553-3639 weekdays 8 a.m. to 4 p.m. CT

Distributed by Kimberly-Clark Global Sales, Inc.,
Dept. XX-XX, PO Box 2020, Neenah, WI 54957-2020
Printed in USA.
Made in the USA from domestic and imported material.

www.kleenex.com

® Registered Trademark and
™ Trademark of Kimberly-Clark Worldwide, Inc.
© 1986, 2003 KCWW
Made under the following US patents:
6,221,211; 5,227,242; 4,828,912; 4,738,847.

This box is made from 100% recycled paper.

EPA Reg. No.: XXXX-XXX
EPA Est. No.: XXXXX-XX-XX

This is so small it can scarcely be seen!

ACTIVE INGREDIENTS:
Citric Acid 7.53%
Sodium Lauryl Sulfate 2.02%
INERT INGREDIENTS 90.45%
Total 100.00%

120 3-PLY TISSUES

10

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

July 25, 2003

MEMORANDUM:

Subject: Efficacy Review EPA Reg.No. 9402-RN *Kleenex Brand Anti-Viral Tissue #2*
DP Barcode 289868 and DP Barcode 289966
Case No.072433

From: Nancy Whyte, Microbiologist NW
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

To: Adam Heyward/Drusilla Copeland
Regulatory Management Branch II
Antimicrobials Division (7510C)

Thru: Emily Mitchell, M.S., Team Leader
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

Thru: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Applicant: Kimberly-Clark Global Sales, Inc.
P. O. Box 2020
Neenah, WI 54957-2020

Formulation Label:

Active Ingredient(s)	%/wt
Citric Acid	7.51%
Sodium lauryl sulfate	2.02%
Other ingredients	90.47%
Total	100.00%

I. Background:

The registrant has submitted an application for a new product registration for a 3-ply tissue which makes claims that the tissue has antiviral properties against Rhinovirus

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Types 1A and 2 and Influenza A Virus and B Virus and Respiratory Syncytial Virus. The tissue makes no claims for antimicrobial action against bacteria or fungi. Two separate versions of the label were submitted--one with the package and a revised label with a disclaimer submitted after a meeting with representatives of the Agency. An additional updated label has been submitted since the revision was reviewed but was not available to this reviewer. This review encompasses two submissions, DP289868 and DP289966, which address issues raised in a pre-registration meeting with the Agency and Kimberly-Clark representatives.

The first package, D289868, contains a cover letter and a revised label. The second package, D289966, contains three articles which support the registrant's rationale for label claims of the product's effectiveness against four viruses known to be implicated in upper respiratory infections. The studies submitted were not conducted using Good Laboratory Practices. The first, MRID No. 459193-01, is a reprint of an article appearing in the *Journal of Infectious Diseases, Vol. 153, No. 2, February 1986,* which reports the results of a study of the interruption of the transmission of rhinovirus colds among human volunteers using virucidal paper handkerchiefs. The second document, MRID No.459193-02, is an article reprint from the same journal (*Vol. 152, August 1985)* which reports on the effect of placebo and virucidal paper handkerchiefs on viral contamination of the hand and transmission of experimental rhinoviral infection. The third document, MRID No. 459193-03, is a private communication which reports the results of virucidal screening studies that were conducted using lotion coating and silicone coating in the outer plies of the tissue to demonstrate complete inactivation of the organisms tested. Five viruses were used in this study--*Rhinovirus 1A, Rhinovirus 2, Influenza Virus A* and *Influenza Virus B,* and *Respiratory Syncytial Virus* . Also included in this document is a table which reports results of several studies conducted in June 2000, January and April 2001, and January 2002. The table lists the results of complete inactivation of the residual viruses by the tissues at various exposure periods when tissues containing either lotion or silicone are used as coatings in the presence of various concentrations of sodium lauryl sulfate and citric acid. This study was conducted by Kimberly-Clark and was reported in April 2003.

II. Use Directions:

There are no specific use directions printed on the box except that "this product is not to be used in a manner inconsistent with its labeling. Use only as a facial tissue to help prevent the spread of colds and flu viruses. "

Iil. Labeling:

1. There are several statements on the overwrap label attached to the box. The largest font type is used to describe the product (**Help Stop the Cycle of Cold & Flu**) The next smaller font is used for an expanded claim for the value of the use of the product.. On the first revision of the label, the disclaimer requested by the Agency, *This product has not been tested against bacteria and fungi,* is listed below the product logo and is printed using much smaller font which is difficult to read.

IV. Recommendations and Comments:

1. The disclaimer required by the Agency that the product has no effectiveness against bacteria, fungi, and other viruses must be elevated above the logo and printed in a font size that is equivalent to the other statements. The statement should be separated on both top and bottom by a space so that consumers will be likely to see and read it.

(112)

LEWIS &
HARRISON
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July 30, 2003

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1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RE
Applicant: Kimberly-Clark Corporation

Dear Adam:

As per our discussion, please find enclosed five (5) copies of a revised product label for Kleenex® Brand Anti-Viral Tissue #2. The label incorporates the changes that you and Connie Welch asked Kimberly-Clark to make.

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

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SUBMISSION BAR CODE # 9631035 REVIEWER D. Copeland

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 9402-EN PM 34 ACTION CODE 188

DESCRIPTOR Chemistry & Efficacy data in response to EPA's ltr dated 11/25/02

[ ] CHILD RESISTANT PACKAGING: [ ] CERTIFICATION
[ ] NON-RESIDENTIAL USE ONLY
[ ] NOT APPLICABLE

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL

PROPOSED CLASSIFICATION: [ ] GENERAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
02 26 03	03 03 03	03 10 03

METHOD OF SUPPORT

[ ] CITE ALL
[ ] SELECTIVE
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

FORMULATORS EXEMPTION

[ ] SUBMITTED
[ ] NOT SUBMITTED
[ ] NOT APPLICABLE
[ ] INCORRECT/RESUB

REVIEW(S) REQUESTED	DATA PACK #	DATE SENT	DUE DATE	DATE RETURNED
CHEMISTRY				
EFFICACY				
TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER _____				

STATUS _____

(114)

RESPONSE CODE 11 RESPONSE DATE 4/30/03

June 30, 2003

Mr. Eliot I. Harrison
Lewis & Harrison Consultant for
Kimberly-Clark Corporation
122 C Street, N.W., Suite 740
Washington, D.C. 20001

Dear Mr. Harrison:

Subject: **Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol Number 9402-RN
Letter Dated February 26, 2003

The labeling referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide and Rodenticide Act, as amended, is ***unacceptable*** for the following reasons:

Proposed Request:

- Application for new product registration

Data deficiencies:

PRODUCT CHEMISTRY Review:

1. The description of the formulation/production process is unacceptable. You made no reference to the addition if the [redacted] and the [redacted] to the formula nor is there a description of the method of application to the [redacted] The process from raw material to finished product is, therefore, incomplete. You must submit to the Agency a detailed description of the formulation/production process including all ingredients in the discussion, the loading of the formulated product onto the [redacted] and quality assurance procedures, where applicable. The discussion may be accompanied by a flow diagram to enhance clarity.

INERT INGREDIENT [illegible] ON IS NOT INCLUDED

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CONCURRENCES								
SYMBOL								
SURNAME								
DATE								

2. The inert ingredients, [redacted] are not on the agency data base of approved inert ingredients for use in pesticide product. Therefore, you must submit or request your suppliers to submit a full disclosure of the chemical composition and character of the inert ingredients. The disclosure must include the name and CAS number of all components, the percent of composition of each component, and a Material Safety Data Sheet for the composition.

3. You submitted a "pre-reaction Confidential Statement of Formula (CSF). The proposed formulation is not an integrated system. Therefore, you must delete it from its supporting documentation of the "pre-reaction CSF." The disclosure of the materials used in the formation of the product must be accomplished in the response to the requirements of OPPTS 830.1600.

Other Comments:

The additional efficacy data/information submitted under a cover letter dated April 25, 2003 is currently in review. Once completed, we will be informed you of the results.

Please respond within 75 days from the date of this letter stating your intentions to comply with the information/data requests cited above. If no resubmission is received during the 75-day period, the application will be administratively withdrawn.

If you have any questions concerning this letter, please contact Adam Heyward at (703) 308-6422 or Drusilla Copeland at (703) 308-6224.

Sincerely,

Adam Heyward
Product Manager (34)
Regulatory Management Branch II
Antimicrobials Division (7510C)

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

May 9, 2003

SUBJECT: PRODUCT CHEMISTRY REVIEW OF: Kleenex Brand Anti-Viral Tissue #2

DP Barcode: D288846 **Reg. No. Or File Symbol: 9402-RN**
Manufacturing-use [ ] OR **End-use Product [X]**

TO: Adam Heyward PM 34 / Drusilla Copeland, Team Reviewer
Regulatory Management Branch II
Antimicrobials Division (7510C)

FROM: Robert A. Turpin, Chemist
Product Science Branch, CT Team
Antimicrobials Division (7510C)

THRU: Karen P. Hicks, CT Team Leader
Product Science Branch
Antimicrobials Division (7510C)

5/14/03

THRU: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Product Formulation

Active Ingredient(s)	**% by wt.**
Citric acid	7.51
Sodium lauryl sulfate	2.02

BACKGROUND: The applicant has submitted, in response to the Agency's request, additional information regarding the formulation process for the subject product and Confidential Statements of Formula representing the pre- and post-reactions. The Product Science Branch has performed the secondary review.

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FINDINGS:

1. The description of the formulation/production process is unacceptable. The applicant makes no reference to the addition of the [redacted] to the formula nor is there a description of the method of application to the [redacted] The process from raw material to finished product is, therefore, incomplete.

2. The inert ingredients, [redacted] are not on the Agency's data base of approved inert ingredients for use in pesticide products.

3. The applicant has submitted to the Agency a "pre-reaction CSF." The formulation of the subject product is not an integrated system.

4. The applicant has included in the Confidential Statement of Formula of the subject product the [redacted] as an inert. [redacted] upon application or use the treatment of the [redacted] in the formulation as an inert is correct.

RECOMMENDATIONS:

1. The applicant must submit to the Agency a detailed description of the formulation/production process including all ingredients in the discussion, the loading of the formulated product onto the [redacted] and quality assurance procedures, where applicable. The discussion may be accompanied by a flow diagram to enhance clarity.

2. The applicant must submit or cause to be submitted a full disclosure of the chemical composition and character of the inert ingredients noted above. The disclosure must include the name and CAS number all components, the percent of composition of each component, and a Material Safety Data Sheet for the composition. The data should be express delivered, e.g., FedEx or UPS, to the Product Manager.

3. The applicant should remove from its support documentation the "pre-reaction CSF." The disclosure of the materials used in the formation of the product should be accomplished in the response to the requirements of OPPTS 830.1600.

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USEPA/OPP PC Code: 021801

- CAS REG. NO. 77-92-9

Synonym(s):

- HYDROXY-1,2,3-PROPANETRICARBOXYLIC ACID
- HYDROXYTRICARBALLYLIC ACID

Scientific Name(s):

- CITRIC ACID

CAS Numbers

- CAS REG. NO. 77-92-9
- 0000077929

List all products for this chemical or, just the active products.
List Unique Registrants (Active/Inactive)

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USEPA/OPP PC Code: 079011

- CAS REG. NO. 151-21-3

Synonym(s):

- DODECYL SULFATE, SODIUM SALT

Scientific Name(s):

- SODIUM LAURYL SULFATE

CAS Numbers

- CAS REG. NO. 151-21-3
- 0000151213

List all products for this chemical or, just the active products.
List Unique Registrants (Active/Inactive)

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DATA EVALUATION RECORD

CITRIC ACID
SODIUM LAURYL SULFATE
(KLEENEX BRAND ANTI-VIRAL TISSUE #2)

STUDY TYPES: **Product Identity and Composition (OPPTS 830.1550)**
Description of Formulation Process (OPPTS 830.1650)
Certified Limits (OPPTS 830.1750)

MRID 45869502

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37830
Action No. K464

Primary Reviewer:
Eric B. Lewis, M.S.
Signature: Eric B. Lewis
Date: APR 17 2003

Secondary Reviewers:
Sylvia Milanez, Ph.D., D.A.B.T.
Signature: Sylvia Milanez
Date: APR 17 2003

Robert H. Ross, M.S., Group Leader
Signature: Robert H. Ross
Date: APR 17 2003

Quality Assurance:
Lee Ann Wilson, M.A.
Signature: L.A. Wilson
Date: APR 17 2003

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

DATE: (April 15, 2003)
SUBJECT: PRODUCT CHEMISTRY REVIEW OF: Kleenex Brand Anti-Viral Tissue #2
DP Barcode: D288846
Reg. No. Or File Symbol: 9402-RN
TGAI/Manufacturing-use Product [ ] OR **End-use Product [x]**

TO: (Team leader/Regulator)
PM Team (#)

FROM: (Reviewer), Chemist, Product Science Branch, CT Team, Antimicrobials Division (7510C)

THRU: Karen P. Hicks, CT Team Leader, Product Science Branch, Antimicrobials Division (7510C)

THRU: Michele E. Wingfield, Chief, Product Science Branch, Antimicrobials Division (7510C)

Product Formulation

Active Ingredient(s)	**% by wt.**
Citric acid	7.51%
Sodium lauryl sulfate	2.02%

I. BACKGROUND: At the Agency's request, the registrant has submitted additional information concerning the formulation process for Kleenex Brand Anti-Viral Tissue #2, along with a "pre-reaction" CSF for the virucidal coating by itself and a "post-reaction" CSF for the finished tissue product.

II. FINDINGS:

1. The description of the formulation process is incomplete. It is not stated how or when the inerts [redacted] are added to the formulation, how the liquid material is applied to the [redacted] or how they are packaged. No information on quality control measures is presented.

2. The registrant submitted "pre-reaction" and "post-reaction" CSFs, but neither adequately reflects the composition of the product to be registered. All the inerts used to formulate the product are not listed on the "pre-reaction" CSF, and the weight of the facial tissue material is included in the composition of the product on the "post-reaction" CSF.

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3. CAS numbers and other information concerning the chemical identity of the inerts [redacted] were not provided on the CSF. The registrant states that this is proprietary information that has been provided to the Agency separately. PC codes were not found for these two inerts.

III. RECOMMENDATIONS:

1. The registrant should submit additional information on the formulation process, detailing how and when [redacted] are added to the formulation and what quality control measures are used.
2. The "pre-reaction" CSF is not needed. The "post-reaction" CSF should include all the active and inert ingredients used to formulate the product, and the sum of these ingredients should be 100%. The [redacted] should not be considered as part of the product, but should be presented in a footnote at the bottom of the CSF. If the registrant wishes to use the submitted product label stating that citric acid is 7.51% and sodium lauryl sulfate is 2.02% of the product, then the CSF should list the nominal concentrations as [redacted] respectively, and column 10 should give the source concentration of sodium lauryl sulfate as [redacted] not [redacted]. It is unclear what the concentrations of the inert ingredients would be when the weight of the [redacted] is excluded from the calculation. The registrant should provide these concentrations on the CSF, and the certified limits for the inerts should be adjusted accordingly once the nominal concentrations of the actives are clarified.
3. The word "proprietary" should be added following the inert components that do not have CAS numbers on the CSF.

IV. PRODUCT CHEMISTRY REVIEW

1. CONFIDENTIAL STATEMENT OF FORMULA (CSF)

1a. Type of manufacturing process and source active ingredient registration

- Non-integrated formulation system (i.e., all TGAI in product are registered) [x]*
  *Assuming acceptable certificates of analysis have been submitted
- Integrated production system [ ]
- if "ME-TOO," specify EPA Reg. # of existing product: _____

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TABLE 1. Product Identity, Composition, and Certified Limits							
Product name: Kleenex Brand Anti-Viral Tissue #2[a]				EPA Reg. #: 9402-RN			
Ingredient name (% purity)	CAS Reg. #	PC Code	EPA Reg. #	Ingredient concentration in product, % w/w			Purpose in formulation
				Nominal	Upper limit	Lower limit	
Citric acid [redacted]				(7.51)	(9.11)	(6.00)	Active
Sodium lauryl sulfate [redacted]				(2.02)	(2.44)	(1.61)	Active
[redacted]							

[a]The [redacted] The final product contains 2.01 lbs of citric acid and 0.54 lbs of sodium lauryl sulfate per [redacted] of tissue.
[b]The remaining [redacted]
[c]Calculated by the reviewer, based on purity of [redacted]
[d]The total concentration of [redacted] used in the formulation of the product is unclear, and needs to be clarified by the registrant.
[e]The concentration on the submitted "post-reaction" CSF is calculated based on the [redacted] being included in the weight of the final product. The registrant should re-calculate the concentration without the weight of the [redacted] and adjust the certified limits accordingly.

1b. Clearance of inerts for non-food or food use:
Cleared for food use under 40 CFR §180.1001: Yes [ ] No [ ] NA [x]

1c. The chemical identity, composition (including that for the TGAI), density, pH, and flammability on the CSF are consistent with guidelines in OPPTS Series 830, Part A and OPPTS 830.7300, 830.7000, and 830.6315 respectively: Yes [ ] No [x]

1d. Nominal Concentrations and Certified Limits for active ingredients are:
Acceptable [ ] Not acceptable [x]

1e. Nominal Concentrations and Certified Limits for inert ingredients are:
Acceptable [ ] Not acceptable [x] Not applicable [ ]

1f. For products produced by an integrated formulation system:
- All impurities of toxicological significance have an Upper Certified Limit?
  Yes [ ] No [ ] Not applicable [x]
- All impurities of $\geq 0.1\%$ in the product have been identified?
  Yes [ ] No [ ] Not applicable [x]

2. PRODUCT LABEL:

2a. The active ingredients statement (chemical IDs and Nominal Concentrations) on the label is consistent with the CSF? Yes [x] No [ ]

2b. The product contains one of the following:

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- 10% or more of a petroleum distillate: Yes [ ] No [x]
- 1.0% or more of methyl alcohol: Yes [ ] No [x]
- Sodium nitrite at any level: Yes [ ] No [x]
- a toxic List 1 inert at any level: Yes [ ] No [x]
- arsenic in any form: Yes [ ] No [x]

2c. If Yes to any of the above, does the inert ingredients statement contain a footnote indicating this? Yes [ ] No [ ] Not applicable [x]

2d. The appropriate warning statement regarding flammability or explosive characteristics of the product are listed on the label? Yes [ ]No [ ] Not applicable [x]

2e. The storage and disposal instructions for the pesticide and container are in compliance with PR Notice 84-1 for household use products or PR Notice 83-3 for all other uses?
Yes [x] No [ ]

2f. Does the product require an expiration date at which time the Nominal Concentration falls below the Lower Certified Limit (based on the one year storage stability data or other information)?
Yes [ ] No [ ]*
*Not addressed in this submission

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3. OPPTS SERIES §830 GUIDELINES

TABLE 2. Product Chemistry Series 830, Part A

OPPTS Guideline	Acceptance of Information*	MRID No.
830.1550 Chemical ID[1]	U	CSF
830.1600 Description of Materials	Not addressed	
830.1620 Production Process[2]	NA	
830.1650 Formulation Process[3]	U	45869502
830.1670 Discussion of Impurities[4]	Not addressed	
830.1700 Preliminary Analysis[5]	Not addressed	
830.1750 Certified Limits[6]	U	CSF
830.1800 Analytical Method for AIs	Not addressed	

*Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; NR= not required, G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

[1]See Table 1 of Product Chemistry Review for additional information.

[2]For MP or EP products manufactured by an integrated production system.

[3]For products manufactured by a non-integrated system (i.e., using a registered TGAI or MP).

[4]May be waived unless actual/possible impurities are of toxicological concern.

[5]Five batch analysis required for products produced by an integrated production system.

[6]If different from standard Certified Limits recommended in 40 CFR 158.175, discussed under "Findings" of the Product Chemistry Review.

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TABLE 3. Product Chemistry Series 830, Part B

Physical/Chemical Properties	Acceptance of data*	Value or qualitative description**	MRID No.
830.6302 Color		Not addressed	
830.6303 Physical State		Not addressed	
830.6304 Odor		Not addressed	
830.6314 Oxidation/Reduction		Not addressed	
830.6315 Flammability/Flash Pt		Not addressed	
830.6316 Explodability		Not addressed	
830.6317 Storage Stability		Not addressed	
830.6320 Corrosion Characteristics		Not addressed	
830.7000 pH		Not addressed	
830.7100 Viscosity		Not addressed	
830.7300 Density/sp. gravity	A	26.77 lb/2880 ft^2 for the finished product	CSF

*Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; NR= Not required G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

**Unless otherwise indicated, the property should be at 25°C.

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DATA EVALUATION RECORD

CITRIC ACID
SODIUM LAURYL SULFATE
(KLEENEX BRAND ANTI-VIRAL TISSUE #2)

STUDY TYPES: **Product Identity and Composition (OPPTS 830.1550)**
Description of Formulation Process (OPPTS 830.1650)
Certified Limits (OPPTS 830.1750)

MRID 45869502

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37830
Action No. K464

Primary Reviewer:
Eric B. Lewis, M.S.
Signature: Eric B. Lewis
Date: APR 17 2003

Secondary Reviewers:
Sylvia Milanez, Ph.D., D.A.B.T.
Signature:
Date: APR 17 2003

Robert H. Ross, M.S., Group Leader
Signature: Robert H. Ross
Date: APR 17 2003

Quality Assurance:
Lee Ann Wilson, M.A.
Signature: L. A. Wilson
Date: APR 17 2003

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
Antimicrobials Division

DATE: (April 15, 2003)
SUBJECT: PRODUCT CHEMISTRY REVIEW OF: Kleenex Brand Anti-Viral Tissue #2
DP Barcode: D288846
Reg. No. Or File Symbol: 9402-RN
TGAI/Manufacturing-use Product [ ] OR **End-use Product [x]**

TO: (Team leader/Regulator)
PM Team (#)

FROM: (Reviewer), Chemist, Product Science Branch, CT Team, Antimicrobials Division (7510C)

THRU: Karen P. Hicks, CT Team Leader, Product Science Branch, Antimicrobials Division (7510C)

THRU: Michele E. Wingfield, Chief, Product Science Branch, Antimicrobials Division (7510C)

Product Formulation

Active Ingredient(s)	**% by wt.**
Citric acid	7.51%
Sodium lauryl sulfate	2.02%

I. **BACKGROUND:** At the Agency's request, the registrant has submitted additional information concerning the formulation process for Kleenex Brand Anti-Viral Tissue #2, along with a "pre-reaction" CSF for the virucidal coating by itself and a "post-reaction" CSF for the finished tissue product.

II. FINDINGS:

1. The description of the formulation process is incomplete. It is not stated how or when the inerts [redacted] are added to the formulation, how the liquid material is applied to the [redacted] or how they are packaged. No information on quality control measures is presented.

2. The registrant submitted "pre-reaction" and "post-reaction" CSFs, but neither adequately reflects the composition of the product to be registered. All the inerts used to formulate the product are not listed on the "pre-reaction" CSF, and the weight of the facial tissue material is included in the composition of the product on the "post-reaction" CSF.

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3. CAS numbers and other information concerning the chemical identity of the inerts [redacted] were not provided on the CSF. The registrant states that this is proprietary information that has been provided to the Agency separately. PC codes were not found for these two inerts.

III. RECOMMENDATIONS:

1. The registrant should submit additional information on the formulation process, detailing how and when [redacted] are added to the formulation and what quality control measures are used.
2. The "pre-reaction" CSF is not needed. The "post-reaction" CSF should include all the active and inert ingredients used to formulate the product, and the sum of these ingredients should be 100%. The [redacted] should not be considered as part of the product, but should be presented in a footnote at the bottom of the CSF. If the registrant wishes to use the submitted product label stating that citric acid is 7.51% and sodium lauryl sulfate is 2.02% of the product, then the CSF should list the nominal concentrations as [redacted] respectively, and column 10 should give the source concentration of sodium lauryl sulfate as [redacted] not [redacted] It is unclear what the concentrations of the inert ingredients would be when the weight of the [redacted] is excluded from the calculation. The registrant should provide these concentrations on the CSF, and the certified limits for the inerts should be adjusted accordingly once the nominal concentrations of the actives are clarified.
3. The word "proprietary" should be added following the inert components that do not have CAS numbers on the CSF.

IV. PRODUCT CHEMISTRY REVIEW

1. CONFIDENTIAL STATEMENT OF FORMULA (CSF)

1a. Type of manufacturing process and source active ingredient registration

- Non-integrated formulation system (i.e., all TGAI in product are registered) [x]*
  *Assuming acceptable certificates of analysis have been submitted
- Integrated production system [ ]
- if "ME-TOO," specify EPA Reg. # of existing product: _____

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TABLE 1. Product Identity, Composition, and Certified Limits							
Product name: Kleenex Brand Anti-Viral Tissue #2[a]				EPA Reg. #: 9402-RN			
Ingredient name (% purity)	CAS Reg. #	PC Code	EPA Reg. #	Ingredient concentration in product, % w/w			Purpose in formulation
				Nominal	Upper limit	Lower limit	
Citric acid [redacted]				(7.51)	(9.11)	(6.00)	Active
Sodium lauryl sulfate [redacted]				(2.02)	(2.44)	(1.61)	Active
[redacted]							

[a]The [redacted] The final product contains 2.01 lbs of citric acid and 0.54 lbs of sodium lauryl sulfate per [redacted] of tissue.
[b]The remaining [redacted]
[c]Calculated by the reviewer, based on purity of [redacted]
[d]The total concentration of [redacted] used in the formulation of the product is unclear, and needs to be clarified by the registrant.
[e]The concentration on the submitted "post-reaction" CSF is calculated based on the [redacted] being included in the weight of the final product. The registrant should re-calculate the concentration without the weight of the [redacted] and adjust the certified limits accordingly.

1b. Clearance of inerts for non-food or food use:
Cleared for food use under 40 CFR §180.1001: Yes [ ] No [ ] NA [x]

1c. The chemical identity, composition (including that for the TGAI), density, pH, and flammability on the CSF are consistent with guidelines in OPPTS Series 830, Part A and OPPTS 830.7300, 830.7000, and 830.6315 respectively: Yes [ ] No [x]

1d. Nominal Concentrations and Certified Limits for <u>active</u> ingredients are:
Acceptable [ ] Not acceptable [x]

1e. Nominal Concentrations and Certified Limits for <u>inert</u> ingredients are:
Acceptable [ ] Not acceptable [x] Not applicable [ ]

1f. For products produced by an integrated formulation system:
- All impurities of toxicological significance have an Upper Certified Limit?
  Yes [ ] No [ ] Not applicable [x]
- All impurities of $\geq 0.1\%$ in the product have been identified?
  Yes [ ] No [ ] Not applicable [x]

2. <u>PRODUCT LABEL:</u>

2a. The active ingredients statement (chemical IDs and Nominal Concentrations) on the label is consistent with the CSF? Yes [x] No [ ]

2b. The product contains one of the following:

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- 10% or more of a petroleum distillate: Yes [ ] No [x]
- 1.0% or more of methyl alcohol: Yes [ ] No [x]
- Sodium nitrite at any level: Yes [ ] No [x]
- a toxic List 1 inert at any level: Yes [ ] No [x]
- arsenic in any form: Yes [ ] No [x]

2c. If Yes to any of the above, does the inert ingredients statement contain a footnote indicating this? Yes [ ] No [ ] Not applicable [x]

2d. The appropriate warning statement regarding flammability or explosive characteristics of the product are listed on the label? Yes [ ]No [ ] Not applicable [x]

2e. The storage and disposal instructions for the pesticide and container are in compliance with PR Notice 84-1 for household use products or PR Notice 83-3 for all other uses?
Yes [x] No [ ]

2f. Does the product require an expiration date at which time the Nominal Concentration falls below the Lower Certified Limit (based on the one year storage stability data or other information)?
Yes [ ] No [ ]*
*Not addressed in this submission

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3. OPPTS SERIES §830 GUIDELINES

TABLE 2. Product Chemistry Series 830, Part A

OPPTS Guideline		Acceptance of Information*	MRID No.
830.1550	Chemical ID[1]	U	CSF
830.1600	Description of Materials	Not addressed	
830.1620	Production Process[2]	NA	
830.1650	Formulation Process[3]	U	45869502
830.1670	Discussion of Impurities[4]	Not addressed	
830.1700	Preliminary Analysis[5]	Not addressed	
830.1750	Certified Limits[6]	U	CSF
830.1800	Analytical Method for AIs	Not addressed	

*Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; NR= not required, G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

[1]See Table 1 of Product Chemistry Review for additional information.

[2]For MP or EP products manufactured by an integrated production system.

[3]For products manufactured by a non-integrated system (i.e., using a registered TGAI or MP).

[4]May be waived unless actual/possible impurities are of toxicological concern.

[5]Five batch analysis required for products produced by an integrated production system.

[6]If different from standard Certified Limits recommended in 40 CFR 158.175, discussed under "Findings" of the Product Chemistry Review.

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TABLE 3. Product Chemistry Series 830, Part B

Physical/Chemical Properties	Acceptance of data*	Value or qualitative description**	MRID No.
830.6302 Color		Not addressed	
830.6303. Physical State		Not addressed	
830.6304 Odor		Not addressed	
830.6314 Oxidation/Reduction		Not addressed	
830.6315 Flammability/Flash Pt		Not addressed	
830.6316 Explodability		Not addressed	
830.6317 Storage Stability		Not addressed	
830.6320 Corrosion Characteristics		Not addressed	
830.7000 pH		Not addressed	
830.7100 Viscosity		Not addressed	
830.7300 Density/sp. gravity	A	26.77 lb/2880 ft^2 for the finished product	CSF

*Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; NR= Not required G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

**Unless otherwise indicated, the property should be at 25° C.

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LEWIS &
HARRISON
Consultants In Government Affairs

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Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

February 26, 2003

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RN
Applicant: Kimberly-Clark Corporation
Registration Application for New Product
Your Letter of November 25, 2002

Dear Adam:

On behalf of Kimberly-Clark Corporation, I responding to your letter of November 25, 2002 regarding Kleenex® Brand Anti-Viral Tissue #2. Responses, including supporting data, to the efficacy and product chemistry deficiencies that were noted in your letter are attached. In addition, human clinical data, that is being submitted pursuant to FIFRA 6(a)(2), is attached.

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

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CHEMISTRY ISSUES:
RESPONSES BY KIMBERLY-CLARK TO AGENCY LETTER DATED NOVEMBER 25, 2002

Product: KLEENEX® BRAND ANTI-VIRAL TISSUE #2
File Symbol No. 9402-RN

Agency Comments 1-7 on page 4 of 11/08/02 Product Chemistry Review
The Confidential Statement of Formula(s) (CSFs) dated 10/14/02 are not acceptable. The CSF consisted of a pre and post-reaction CSF. The registrant should clarify that the post-reaction CSF is based on [redacted] when in the pre-reaction CSF they produce a total weight of [redacted] The registrant must type "List 4" under the column for the AI citric acid. The registrant should type "post-reaction" in addition to the product name in box 3 in the post-reaction CSF. The registrant needs to provide the CAS Numbers for [redacted] on the CSF. The registrant should report the purity of the SLS in the post-reaction CSF.

Kimberly-Clark Response
Revised pre (virucidal coating) and post-reaction (finished product) CSFs are attached. In the post-reaction CSF, "box 13" now specifies the amount of ingredient added per area (lb/ft^2). In addition, List 4 has been placed under "column 10" for both active ingredients - citric acid and SLS. The terms pre and post reaction have been added in "box 3" under the product name. CAS numbers have not been added to the CSF for the inert ingredients, [redacted] since only the regulatory staff at Kimberly-Clark has been permitted by the inert supplier to have access the actual components on these inerts. However, as noted below, the CAS numbers for each component of [redacted] have been submitted to the Agency. The purity of SLS, as indicated in the post-reaction CSF, is 100%.

Agency Comment # 8, on page 4 of 11/08/02 Product Chemistry Review
The registrant needs to provide the following information for the inert ingredients, [redacted] and [redacted]

- CAS Numbers for all components
- Chemical names of all components.
- Percentage amount of each of the components in the inert formulation. The total must equal 100% although ranges are acceptable.

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Kimberly-Clark Response
As discussed at the meeting on 1/22/03 the requested information on the inert ingredients was previously submitted to the Agency. In addition, copies of the previously submitted informtion was provided directly to Juan Negron during the meeting.

Agency Comment#3 on Formulation Process, pg 7 of 11/08/02 Product Chemistry Review
The formulation process requires upgrading

Kimberly-Clark Response
As agreed to at the 1/22/03 meeting, Kimberly-Clark is submitting a description of the formulation process for the virucidal coating material. A document presenting this material is attached.

458695-00

LEWIS & HARRISON
Consultants In Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

February 26, 2003

Adam Heyward Product Manager (34)
Regulatory Management Branch II
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RN
Applicant: Kimberly-Clark Corporation
Registration Application for New Product
Data Transmittal Letter for Studies being Submitted in Response to Your Correspondence of November 25, 2002

Dear Adam:

On behalf of Kimberly-Clark Corporation, I am submitting three copies of the following studies in response to your correspondence of November 25, 2002:

Efficacy

- Volume 1 of 1
  Discussion of Soil Load Used in Virucidal Studies Conducted with Kleenex® Brand Anti-Viral Tissue #2
  MRID# 45869501

Product Chemistry

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- Kleenex® Brand Anti-Viral Tissue #2: Formulation Process for Virucidal Coating Solution
  MRID# 45869502

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

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EFFICACY ISSUES:
RESPONSES BY KIMBERLY-CLARK TO AGENCY LETTER DATED NOVEMBER, 25 2002

Product: Kleenex® Brand Anti-Viral Tissue #2.
File Symbol No. 9402-RN

Agency Comment #1

EPA's standards for environmental surfaces are hard, inanimate surfaces, either porous or non-porous. Based on study methodology, the tissue itself (as opposed to a human face or nose) is the surface of interest. A facial tissue is porous and is also soft.

Kimberly-Clark Response

Regarding the above comment, it is important to note that a meeting was held on February 6, 2001 between Antimicrobial Division (AD) staff and Kimberly-Clark representatives to discuss the registration application for Kleenex® Brand Anti-Viral Tissue #2. The efficacy protocol was discussed in detail at the meeting and AD staff did not express any significant concerns about the protocol. In fact, AD staff stated that the protocol was fundamentally sound (see attached "Summary of Meeting" and AD follow-up letter). It should also be noted that the protocol used to evaluate the efficacy of Kleenex® Brand Anti-Viral Tissue #2 is practically identical to the protocol that was used to support the registration of Kimberly-Clark's previously registered antiviral tissue product, Avert, EPA Reg. No. 9402-3.

Agency Comment #2

The study against Rhinovirus 2 did not meet the DIS/TSS-7 requirement that the recoverable virus titer must be at least 10^4.

Kimberly-Clark Response

The initial virus titer used in the Rhinovirus 2 study was 10^5. However, when the virus was applied and dried on the tissue an average of 3 replicate trials showed a $10^{3.6}$ virus survival on the untreated tissue control. Because there was no cytotoxicity found in the first dilution, there was sufficient virus to demonstrate a 3-log reduction and complete virus inactivation. Even though Kimberly-Clark believes that the Rhinovirus 2 study is valid, a new study has been conducted to conclusively demonstrate that Kleenex® Brand Anti-Viral Tissue #2 is efficacious against this virus. The new study, which will be submitted shortly, showed complete inactivation of virus with a log-reduction greater than 4.

Agency Comment #3

The product has not been tested as a disinfectant (i.e., successfully tested against bacteria *Salmonella choleraesuis* and *Staphylococcus aureus*, with or without *Pseudomonas aeruginosa*. Although three product lots (including a 60-day old lot) were tested in the virucidal studies provided in this data package, the Agency will not register a product tested merely as a virucide without having met the basic disinfectant claims in DIS/TSS-1.

Kimberly-Clark Response

Kimberly-Clark has several comments on this issue. First, the proposed product label and efficacy protocol was sent to AD well in advance of the February 6, 2001 meeting and was extensively discussed at the meeting. There was no indication at the meeting or in follow-up correspondence that the Agency wanted an antiviral tissue product to be tested against bacteria. Secondly, Kleenex® Brand Anti-Viral Tissue #2 is a dry tissue that will be packaged in a standard tissue box. The product is not similar to the pre-moistened disinfectant wipes. Accordingly, it is extremely unlikely that Kleenex® Brand Anti-Viral Tissue #2 will be used by consumers in any manner other than as a nasal tissue. Thirdly, the product is solely intended to control cold and flu viruses that may be present in nasal secretions. Although bacteria may also be present in nasal secretions, there is no information to suggest that bacteria associated with nasal secretions are a public-health issue. In this regard, it is important to note that over the past several years, the Agency has expressed significant concerns about superfluous antimicrobial claims, particularly when there is no evidence that the target microbial contamination is of public-health concern. To require Kleenex® Brand Anti-Viral Tissue #2 be tested against bacteria when the product is not intended to be antibacterial and bacterial control is not a public-health concern seems inconsistent with the Agency's desired position. Finally, having anti-bacterial claims on an antiviral tissue may lead consumers to associate colds and flu with bacteria. Such an association will clearly have negative public-health implications since it may lead to increased requests for antibiotic use.

Agency Comment #4

An organic soil load was not mentioned in any of the studies. Although viral inoculum is frequently accompanied by some naturally occurring organic soil (e.g. serum), in actual use, the product would be challenged with 100 percent soil load (e.g. nasal mucus, eye discharge, phlegm, and/or sputum). You must provide data about the nature and concentration of the organic soil load challenge (if any) employed in these studies.

Kimberly-Clark Response
The organic soil load issue is addressed in the attached study ("Discussion of Soil Load Used in Virucidal Studies Conducted with Kleenex® Brand Anti-Viral Tissue #2"). In brief, a soil load was used in the virucidal studies and the load was consistent with the level that would be encountered during actual consumer use.

Agency Comment #5
The proposed label claims indicate that the product can be used in hospital settings. A mere virucide cannot make this claim. No efficacy data was submitted to support claims against *Pseudomonas aeruginosa* which is an Agency requirement for a hospital disinfectant claim.

Kimberly-Clark Response
The product will only be used in hospital settings, as an antiviral tissue, to control the transmission of cold and flu viruses. For the reasons articulated above in response number 3, there is no scientific reason for testing the product against bacteria.

Agency Comment #6
The claim for 15 minutes is questionable. A tissue is usually disposed of in 1 or 2 minutes after use. A more appropriate time would be 30 seconds.

Kimberly-Clark Response
Kimberly-Clark concurs with the Agency that a 30 second claim would be optimal. In this regard, it should be noted that unsubmitted studies conducted by Kimberly-Clark showed significant, but not complete, inactivation, within 1 minute.

The previously submitted consumer survey report (MRID # 45722901), showed that a considerable number of individuals do not rapidly dispose of used tissues. In addition, there are many situations (i.e. church, classrooms, movie theaters, etc.) in which used tissues cannot be immediately disposed. Consequently, the 15-minute contact time for complete viral inactivation will be pertinent to a significant part of the population, particularly since there are no other currently registered antiviral tissues.

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EPA Reg# 9402-10

Page____ is not included in this copy.

Pages 143 through 145 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

✓ Documents Claimed Confidential by the Registr

The information not included is generally considered confidentia by product registrants. If you have any questions, please contac the individual who prepared the response to your request.

EPA Reg # 9462-10

Page____ is not included in this copy.

Pages 146 through 147 are not included.

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EPA Reg #9402-10

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EFFICACY ISSUES:
RESPONSES BY KIMBERLY-CLARK TO AGENCY LETTER DATED NOVEMBER, 25 2002

Product: Kleenex® Brand Anti-Viral Tissue #2.
File Symbol No. 9402-RN

Agency Comment #1
EPA's standards for environmental surfaces are hard, inanimate surfaces, either porous or non-porous. Based on study methodology, the tissue itself (as opposed to a human face or nose) is the surface of interest. A facial tissue is porous and is also soft.

Kimberly-Clark Response
Regarding the above comment, it is important to note that a meeting was held on February 6, 2001 between Antimicrobial Division (AD) staff and Kimberly-Clark representatives to discuss the registration application for Kleenex® Brand Anti-Viral Tissue #2. The efficacy protocol was discussed in detail at the meeting and AD staff did not express any significant concerns about the protocol. In fact, AD staff stated that the protocol was fundamentally sound (see attached "Summary of Meeting" and AD follow-up letter). It should also be noted that the protocol used to evaluate the efficacy of Kleenex® Brand Anti-Viral Tissue #2 is practically identical to the protocol that was used to support the registration of Kimberly-Clark's previously registered antiviral tissue product, Avert, EPA Reg. No. 9402-3.

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The study against Rhinovirus 2 did not meet the DIS/TSS-7 requirement that the recoverable virus titer must be at least 10^4.

Kimberly-Clark Response
The initial virus titer used in the Rhinovirus 2 study was 10^5. However, when the virus was applied and dried on the tissue an average of 3 replicate trials showed a $10^{3.6}$ virus survival on the untreated tissue control. Because there was no cytotoxicity found in the first dilution, there was sufficient virus to demonstrate a 3-log reduction and complete virus inactivation. Even though Kimberly-Clark believes that the Rhinovirus 2 study is valid, a new study has been conducted to conclusively demonstrate that Kleenex® Brand Anti-Viral Tissue #2 is efficacious against this virus. The new study, which will be submitted shortly, showed complete inactivation of virus with a log-reduction greater than 4.

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The product has not been tested as a disinfectant (i.e., successfully tested against bacteria *Salmonella choleraesuis* and *Staphylococcus aureus*, with or without *Pseudomonas aeruginosa*. Although three product lots (including a 60-day old lot) were tested in the virucidal studies provided in this data package, the Agency will not register a product tested merely as a virucide without having met the basic disinfectant claims in DIS/TSS-1.

Kimberly-Clark Response

Kimberly-Clark has several comments on this issue. First, the proposed product label and efficacy protocol was sent to AD well in advance of the February 6, 2001 meeting and was extensively discussed at the meeting. There was no indication at the meeting or in follow-up correspondence that the Agency wanted an antiviral tissue product to be tested against bacteria. Secondly, Kleenex® Brand Anti-Viral Tissue #2 is a dry tissue that will be packaged in a standard tissue box. The product is not similar to the pre-moistened disinfectant wipes. Accordingly, it is extremely unlikely that Kleenex® Brand Anti-Viral Tissue #2 will be used by consumers in any manner other than as a nasal tissue. Thirdly, the product is solely intended to control cold and flu viruses that may be present in nasal secretions. Although bacteria may also be present in nasal secretions, there is no information to suggest that bacteria associated with nasal secretions are a public-health issue. In this regard, it is important to note that over the past several years, the Agency has expressed significant concerns about superfluous antimicrobial claims, particularly when there is no evidence that the target microbial contamination is of public-health concern. To require Kleenex® Brand Anti-Viral Tissue #2 be tested against bacteria when the product is not intended to be antibacterial and bacterial control is not a public-health concern seems inconsistent with the Agency's desired position. Finally, having anti-bacterial claims on an antiviral tissue may lead consumers to associate colds and flu with bacteria. Such an association will clearly have negative public-health implications since it may lead to increased requests for antibiotic use.

Agency Comment #4

An organic soil load was not mentioned in any of the studies. Although viral inoculum is frequently accompanied by some naturally occurring organic soil (e.g. serum), in actual use, the product would be challenged with 100 percent soil load (e.g. nasal mucus, eye discharge, phlegm, and/or sputum). You must provide data about the nature and concentration of the organic soil load challenge (if any) employed in these studies.

Kimberly-Clark Response
The organic soil load issue is addressed in the attached study ("Discussion of Soil Load Used in Virucidal Studies Conducted with Kleenex® Brand Anti-Viral Tissue #2"). In brief, a soil load was used in the virucidal studies and the load was consistent with the level that would be encountered during actual consumer use.

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The proposed label claims indicate that the product can be used in hospital settings. A mere virucide cannot make this claim. No efficacy data was submitted to support claims against *Pseudomonas aeruginosa* which is an Agency requirement for a hospital disinfectant claim.

Kimberly-Clark Response
The product will only be used in hospital settings, as an antiviral tissue, to control the transmission of cold and flu viruses. For the reasons articulated above in response number 3, there is no scientific reason for testing the product against bacteria.

Agency Comment #6
The claim for 15 minutes is questionable. A tissue is usually disposed of in 1 or 2 minutes after use. A more appropriate time would be 30 seconds.

Kimberly-Clark Response
Kimberly-Clark concurs with the Agency that a 30 second claim would be optimal. In this regard, it should be noted that unsubmitted studies conducted by Kimberly-Clark showed significant, but not complete, inactivation, within 1 minute.

The previously submitted consumer survey report (MRID # 45722901), showed that a considerable number of individuals do not rapidly dispose of used tissues. In addition, there are many situations (i.e. church, classrooms, movie theaters, etc.) in which used tissues cannot be immediately disposed. Consequently, the 15-minute contact time for complete viral inactivation will be pertinent to a significant part of the population, particularly since there are no other currently registered antiviral tissues.

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EPA Reg # 9402-10

Page____ is not included in this copy.

Pages 153 through 155 are not included.

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____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

✓ The document is a duplicate of page(s) 143-145.

____ The document is not responsive to the request.

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EPA Reg # 9402-10

Page____ is not included in this copy.

Pages 156 through 157 are not included.

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SUBMISSION BAR CODE # 5619396 REVIEWER D. Copeland

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 9402-RN PM 34 ACTION CODE 187

DESCRIPTOR Application for End-Use Product

[ ] CHILD RESISTANT PACKAGING: [ ] CERTIFICATION
[ ] NON-RESIDENTIAL USE ONLY
[ ] NOT APPLICABLE

REGISTRATION TYPE: [ ] CONDITIONAL [ ] UNCONDITIONAL

PROPOSED CLASSIFICATION: [ ] GENERAL [ ] RESTRICTED USE

DATE ON APPLICATION	EPA RECEIVE DATE	PM RECEIVE DATE
7 5 02	7 29 02	7 29 02

~~METHOD OF SUPPORT~~

[ ] ~~CITE ALL~~
[ ] ~~SELECTIVE~~
[ ] ~~NOT SUBMITTED~~
[ ] ~~NOT APPLICABLE~~
[ ] ~~INCORRECT/RESUB~~

~~FORMULATORS EXEMPTION~~

[ ] ~~SUBMITTED~~
[ ] ~~NOT SUBMITTED~~
[ ] ~~NOT APPLICABLE~~
[ ] ~~INCORRECT/RESUB~~

REVIEW(S) REQUESTED	DATA PACK #	~~DATE SENT~~	~~DUE DATE~~	~~DATE RETURNED~~
CHEMISTRY				
EFFICACY				
TOXICOLOGY				
HED TOX.				
ENVIRON. FATE				
FISH/WILDLIFE				
OTHER _____				

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STATUS _____

RESPONSE CODE 13

NOV 25 2002

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
Washington, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

November 25, 2002

Mr. Eliot I. Harrison
Lewis & Harrison Consultant for
Kimberly-Clark Corporation
122 C Street, N.W., Suite 740
Washington, D.C. 20001

Dear Mr. Harrison:

Subject: **Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol Number 9402-RN
Application Dated: July 5, 2002
EPA Receipt Date: July 7, 2002

The labeling referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide and Rodenticide Act, as amended, is ***unacceptable*** for the following reasons:

Proposed Request:

- Application for new product registration

Data deficiencies:

I. ***Efficacy Review:***

The proposed label claims are not acceptable regarding the use of the proposed product, "Kleenex Brand Anti-Viral Tissue #2," as a Virucide against Rhinovirus 1A and 2, Influenza A and B, and Respiratory Syncytial Virus for a contact time of 15 minutes. The study against Rhinovirus 2 did not meet the DIS/TSS-7 requirements in that the recoverable virus titer must be at least 104. Furthermore, the Agency standards for impregnated towelettes for hard surface disinfection do not apply to this impregnated facial tissue for reasons listed below.

- The EPA's standards for environmental surfaces are hard, inanimate surfaces, either porous or non-porous. Based on the study methodology, the tissue itself (as opposed to a human face or nose) is the surface of interest. A facial tissue is porous and is also soft.

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- The product has not been tested as a disinfectant (i.e., successfully tested against bacteria *Salmonella choleraesuis* and *Staphylococcus aureus*, with or without *Pseudomonas aeruginosa*). Although three product lots (including a 60-day-old lot) were tested in the virucidal studies provided in this data package, the Agency will not register a product tested merely as a virucide without having met the basic disinfectant claims in DIS/TSS-1.

- An organic soil load was not mentioned in any of the studies. Although viral inoculum is frequently accompanied by some naturally-occurring organic soil (e.g., serum), in actual use, the product would be challenged with 100 percent organic soil load (e.g., nasal mucus, eye discharge, phlegm, and/or sputum). You must provide data about the nature and concentration of the organic soil load challenge (if any) employed in these studies.

- The proposed label claims indicate that the product can be used in hospital settings. A mere virucide cannot make that claim. No efficacy data was submitted to support claims against *Pseudomonas aeruginosa*, which is an Agency requirement for a hospital disinfectant claim.

- The claim for 15 minutes is questionable. A tissue is usually disposed of in 1 or 2 minutes after use. A more appropriate contact time would be 30 seconds.

Other questionable labeling comments:

- The phrases [see page 2 of the label], implying "newness," include: "NOW with" and "Introducing a revolution in facial tissues."

- The repeated use of percent kill (99.9%) on the proposed label [see page 2 of the label]; although accurate, this is not the Agency's virucidal performance standard in the absence of cytotoxicity.

- The proposed label repeatedly indicates the product's ability to "kill 99.9% of virus*" [see page 2 of the label]; this is an incomplete phrase and is not acceptable. However, "kill virus* on the used facial tissue in 15 minutes" may be more acceptable.

- Optional terms suggested on the proposed label [see page 3 of the label] include "clinically" testing efficacy; only non-clinical (i.e., no human subject) efficacy study reports were provided with this data package.

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II ***Product chemistry:***

The Confidential Statement of Formula of Formula (CSF) dated October 10, 2002 and product chemistry dated submitted in support of the proposed product are not acceptable. You must address all of the deficiencies listed in the attached product chemistry review dated November 19, 2002. In addition, you must submit or request your supplier to submit the chemical identity of the inerts, [redacted] and [redacted]

Acceptable data:

Acute Toxicity:

The acute toxicity data submitted is acceptable. The current acute toxicity database regulatory status for the subject product is summarized in the table below.

Data Requirement	Means of Support	Status/ Tox Category
Acute Oral Toxicity	MRID #457138-06	Acceptable/Tox category IV
Acute Dermal Tox.	MRID #457138-07	Acceptable/Tox category IV
Acute Inhalation Tox.	Waive Request	Acceptable/Waiver
Eye Irritation	MRID #457138-08	Acceptable/Tox category IV
Skin Irritation	MRID #457138-09	Acceptable/Tox category IV
Skin Sensitization	MRID #457138-10	Acceptable/Non-Sensitizer

Note that, based on rationale provided in your application, the Agency has waived the "the Child signal word and Keep out of reach of children" statements. The waiver is permitted under § 40 CFR 156.66(b)(2), since the product presumably will be used on children. In addition, your letter dated July 5, 2002 details several points in support of your request for a waiver.

Other Comments:

The policy on antimicrobial towellettes and wipes is under consideration by the Antimicrobials Division. Once the policy has been finalized, you will be informed if there are any changes that need to be made regarding the registration process and if there are any additional data that must be submitted to the Division for review.

For detailed information and considerations, please refer to the enclosed EPA/AD Product Science Branch review (product chemistry, efficacy and acute toxicity) reviews.

Please respond within 75 days from the date of this letter stating your intentions to comply with the information/data requests cited above. If no resubmission is received during the 75-day period, the application will be administratively withdrawn.

If you have any questions concerning this letter, please contact Adam Heyward at (703) 308-6422 or Drusilla Copeland at (703) 308-6224.

Sincerely,

Adam Heyward
Product Manager (34)
Regulatory Management Branch II
Antimicrobials Division (7510C)

Enclosures: Product Chemistry, Efficacy and Precautionary Labeling Reviews

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

November 19, 2002

MEMORANDUM

Subject: Data Package D284617
Kleenex® Brand Anti-Viral Tissue #2, EPA File Symbol 9402-RN

From: Wallace Powell, Biologist
Product Science Branch
Antimicrobials Division (7510C)

Through: Karen P. Hicks, Team Leader
Chemistry/Toxicology Team
Product Science Branch
Antimicrobials Division (7510C)

Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

To: Adam Heyward, Product Manager, Team 34
Drusilla Copeland, Team Reviewer, Team 34
Regulatory Management Branch II
Antimicrobials Division (7510C)

BACKGROUND

The applicant, Kimberly-Clark Corporation (as represented by an agent), has submitted a package for registration of the subject product, Kleenex® Brand Anti-Viral Tissue #2. The active ingredients are citric acid (7.51% of product contents by weight) and sodium lauryl sulfate (2.02% by weight).

The submitted package includes studies for acute oral toxicity, acute dermal toxicity, eye irritation, skin irritation, and skin sensitization – MRID's 457138-06 through 457138-10, respectively. The studies were initially reviewed for Product Science Branch (PSB) by Oak Ridge National Laboratory. The reviews are attached to this memorandum. The submitted package also includes an acute inhalation toxicity data waiver request.

DISCUSSION AND RECOMMENDATION

The submitted studies are acceptable. The test material identified in the study reports represents the subject product. The resulting acute Toxicity Categories are listed in the table below. (The attached review of the skin sensitization study has been edited by PSB to indicate acceptability, as PSB has now received a copy of the missing positive control data.)

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Acute oral toxicity.. The submitted study is acceptable. Due to the nature of the test substance, it was not considered possible to dose the animals via gavage at sufficient volumes to achieve the 5 g/kg dosage. Consequently, the ground test substance was mixed with peanut butter and fed to the animals during a 24 hour period. This is acceptable. According to the guidelines (OPPTS 870.1100), "If a single dose is not possible, the dose may be given in smaller fractions over a period not exceeding 24 hours."

Acute dermal toxicity. The submitted study is acceptable.

Acute inhalation toxicity. The waiver request is acceptable. The product does not contain expressible liquid. In view of this, the citric acid and sodium lauryl sulfate are not present in high enough concentrations to present an acute hazard. Also note that the estimated vapor pressure of sodium lauryl sulfate is extremely low.

Eye irritation. The submitted study is acceptable. 'Positive' degree of irritation was limited to moderate swelling (grade 2 on the Draize scale) in one out of three test animals at 1 Hour and cleared by 24 Hours.

Skin irritation. The submitted study is acceptable. As stated in the attached study review, "The guideline requires 0.5 mL of liquid or 500 mg of solid or semisolid applied to the test site. The study author did not indicate the weight of the 2.5 cm x 2.5 cm test material. This deviation would not affect the results." The dosage was a patch cut out of a sheet of the tissue. Based on the bulk density of the product, it would take approximately 17 such patches to amount to 500 mg. Normally this could be problematic. In the present case, however, the study can reasonably be accepted for the following reasons. (1) Exposure to 17 tissue thicknesses for a lengthy time is not realistic in the real world. (2) Each patch is three-ply. Two of the plies are treated with lotion. The third ply contains the antimicrobial chemicals which, if 17 patches were used, would have to migrate through the other two lotion-treated plies of each underlying patch in order to reach the test animal. It is unlikely that the test animals' exposure to the antimicrobial chemicals would be increased greatly by having multiple patches. (3) Since no dermal irritation was noted on any test animal in the study, no more than mild skin irritation at worst would be expected to result from the addition of patches. Also note that no skin irritation was noted in the acute dermal toxicity study.

Skin sensitization. The submitted study is acceptable. The required historical positive control study was not included with the original study report, but one was later cited (MRID 455757-09) and a copy was Faxed to Product Science Branch at EPA. The test results were appropriate.

Summary. The updated acute toxicity regulatory profile is listed in the table below.

Table: Acute toxicity regulatory status for Kleenex® Brand Anti-Viral Tissue #2

Data Requirement	Means of Support	Status
Acute Oral Toxicity	MRID 457138-06, submitted	Acceptable, Tox Category IV
Acute Dermal Tox.	MRID 457138-07, submitted	Acceptable, Tox Category IV
Acute Inhalation Tox.	Waiver request	Acceptable, Waived
Eye Irritation	MRID 457138-08, submitted	Acceptable, Tox Category IV
Skin Irritation	MRID 457138-09, submitted	Acceptable, Tox Category IV
Skin Sensitization	MRID 457138-10, submitted	Acceptable, Non-sensitizer

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Product labeling – precautionary statements

PSB has no adverse comments to the proposed label (EPA Received date 09/13/2002) in regard to human-hazard precautionary or first-aid statements. None appear on the label, and it is PSB's opinion that none are required.

The label for this product is not required to display a Signal Word (as per 40 CFR 156.64).

In response to the applicant's request and rationale, PSB recommends a waiver of the "Keep out of reach of children" child hazard warning. The waiver is permitted by 40 CFR 156.66(b)(2), since the product presumably will be accepted for use on children (unless Risk Assessment and Science Support Branch has objected to this). The applicant's letter (Eliot Harrison to Adam Heyward, 07/05/2002) details several additional points of rationale. These points include an Agency classification of the product's active ingredients; a reference to consumer products which contain one or other of these active ingredients and involve exposure to children; absence of adverse effects reports involving exposure of children to these active ingredients; absence of adverse effects reports from the applicant's own consumer reporting system involving exposure of children to another of the applicant's consumer tissue products that is said to contain similar inert ingredients; and the futility of placing a child prohibition on a widely marketed box of facial tissues.

DATA EVALUATION RECORD

CITRIC ACID
(2371.01)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT
[OPPTS 870.1100 (§81-1)] OECD 401
MRID 45713806

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K402

Primary Reviewer:
Susan Chang, M.S.

Signature: Susan Chang
Date: SEP 1 1 2002

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.

Signature: H T Borges
Date: SEP 1 1 2002

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: SEP 1 1 2002

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: SEP 1 1 2002

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Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1, 870.1100)

Product Manager: Adam Heyward
Reviewer: Susan Chang
MRID No.: 45713806
Study Completion Date: June 3, 2002

Report No.: MB 02-10017.01

Testing Laboratory: MB Research Laboratories
Author: Daniel R. Cerven

GLP Compliance Statement (40 CFR §160.12): Included

Test Material: 2371.01 (Kleenex Brand Anti-Viral Tissue #2), white tissue with blue dots
Dosage: 5000 mg/kg
Species: Wistar rats (5 M and 5 F)
Weight: Males: 206-213 g, Females: 203-239 g **Age**: Approximately 7-10 weeks
Source: Ace Animals, Boyertown, PA

Summary:

1. **LD_{50} (mg/kg):** **Males** > 5000 mg/kg
   Females > 5000 mg/kg
   Combined > 5000 mg/kg
2. **The estimated LD_{50} is** > 5000 mg/kg.
3. **Tox. Category**: IV **Classification**: Acceptable

Procedure (Deviations from §81-1, 870.1100): The ground test material mixed with peanut butter was fed to the animals during a 24 hour period.

Results:

Reported Mortality			
Dosage (mg/kg)[a]	(Number Deaths/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

[a]20 g of ground test material was mixed with 180 g of peanut butter.

Observations: All animals survived, gained weight, and had no abnormal physical signs during the study.

Gross Necropsy Findings: Necropsy results were normal.

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DATA EVALUATION RECORD

CITRIC ACID
(2372.01)

STUDY TYPE: ACUTE DERMAL TOXICITY - RABBIT
[OPPTS 870.1200 (§81-2)] OECD 402
MRID 45713807

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K402

Primary Reviewer:
Susan Chang, M.S.

Signature: S. Chang
Date: SEP 11 2002

Secondary Reviewers:
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Signature: H.T. Borges
Date: SEP 11 2002

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: SEP 11 2002

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: SEP 11 2002

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: Adam Heyward
Reviewer: Susan Chang
MRID No.: 45713807
Study Completion Date: June 3, 2002

Report No.: MB 02-10019.02

Testing Laboratory: MB Research Laboratories
Author: Daniel R. Cerven

GLP Compliance Statement (40 CFR §160.12): Included

Test Material: 2372.01 (Kleenex Brand Anti-Viral Tissue #2), white tissue with blue dots
Dosage: 5000 mg/kg (dry weight of the test material)

Species: New Zealand White rabbits (5M and 5F)
Weight: Males: 2.0-2.4 kg, Females: 2.0-2.3 kg
Age: Approximately 9.5 weeks
Source: Millbrook Breeding Labs, Amherst, MA

Summary:

1. **LD_{50} (mg/kg)**: **Males** > 5000 mg/kg
   Females > 5000 mg/kg
   Combined > 5000 mg/kg
2. **The estimated LD_{50} is** > 5000 mg/kg.
3. **Tox. Category**: IV **Classification**: Acceptable

Procedure (Deviation From §81-2, 870.1200): No deviations were noted.

Results:

Reported Mortality			
Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: All animals survived, gained weight, and all appeared normal throughout the study. No dermal irritation was noted during the study.

Gross Necropsy Findings: Necropsy results were normal.

Note: The test material was identified as 2372.02 on page 5 and 6, but as 2372.01 on other pages in the study report (MRID 45713807). This discrepancy would not affect the results of the study.

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DATA EVALUATION RECORD

CITRIC ACID
(2374.01)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT
[OPPTS 870.2400 (§81-4) OECD 405
MRID 45713808

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K402

Primary Reviewer:
Susan Chang, M.S.

Signature:
Date: SEP 1 1 2002

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.

Signature:
Date: SEP 1 1 2002

Robert H. Ross, M.S., Group Leader

Signature:
Date: SEP 1 1 2002

Quality Assurance:
Lee Ann Wilson, M.A.

Signature:
Date: SEP 1 1 2002

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DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: Adam Heyward
Reviewer: Susan Chang
MRID No.: 45713808
Study Completion Date: May 7, 2002

Report No.: MB 02-10023.04

Testing Laboratory: MB Research Laboratories
Author: Daniel R. Cerven

GLP Compliance Statement (40 CFR §160.12): Included

Test Material: 2374.01 (Kleenex Brand Anti-Viral Tissue #2), white tissue with blue dots
Dosage: 0.1 mL (= 27 mg)

Species: New Zealand White rabbits (3M)
Weight: Males: 2.3-2.9 kg
Age: Approximately 3 months
Source: Millbrook Breeding Labs, Amherst, MA

Summary:

1. **Toxicity Category**: IV
2. **Classification**: Acceptable

Procedure (Deviations From §81-4, 870.2400): None.

Results:

Observations	Number "Positive"/Number Tested			
	Hour			
	1	24	48	72
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae				
Redness	0/3	0/3	0/3	0/3
Chemosis	1/3	0/3	0/3	0/3
Discharge	0/3	0/3	0/3	0/3

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DATA EVALUATION RECORD

CITRIC ACID
(2373.01)

STUDY TYPE: PRIMARY SKIN IRRITATION - RABBIT
[OPPTS 870.2500 (§81-5)] OECD 404
MRID 45713809

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K402

Primary Reviewer:
Susan Chang, M.S.

Signature: S Chang
Date: SEP 11 2002

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.

Signature: H T Borges
Date: SEP 11 2002

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: SEP 11 2002

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: SEP 11 2002

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DATA REVIEW FOR PRIMARY SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: Adam Heyward
Reviewer: Susan Chang
MRID No.: 45713809
Study Completion Date: May 7, 2002

Report No.: MB 02-10021.03

Testing Laboratory: MB Research Laboratories
Author: Teresa Hoff

GLP Compliance Statement (40 CFR §160.12): Included

Test Material: 2373.01 (Kleenex Brand Anti-Viral Tissue #2), white tissue with blue dots
Dosage: 2.5 cm x 2.5 cm patch of the test material

Species: New Zealand White rabbits (1M and 2F)
Weight: Male: 2.3 kg, Females: 2.3-2.4 kg **Age**: Approximately 3 months
Source: Millbrook Breeding Labs, Amherst, MA

Summary:

1. **Toxicity Category**: IV
2. **Classification**: Acceptable

Procedure (Deviations From §81-5, 870.2500): The guideline requires 0.5 mL of liquid or 500 mg of solid or semisolid applied to the test site. The study author did not indicate the weight of the 2.5 cm x 2.5 cm test material. This deviation would not affect the results.

Results: No dermal irritation was noted on any rabbit throughout the study.

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DATA EVALUATION RECORD

CITRIC ACID
(2375.01)

STUDY TYPE: SKIN SENSITIZATION - GUINEA PIG
[OPPTS 870.2600 (§81-6) OECD 406
MRID 45713810

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K402

Primary Reviewer:
Susan Chang, M.S.

Signature: Susan Chang
Date: SEP 1 1 2002

Secondary Reviewers:
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Signature: H.T Borges
Date: SEP 1 1 2002

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: SEP 1 1 2002

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: SEP 1 1 2002

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Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: Adam Heyward
MRID No.: 45713810

Reviewer: Susan Chang
Study Completion Date: June 17, 2002

Report No.: MB 02-10025.06

Testing Laboratory: MB Research Laboratories
Author: Debra Hall

GLP Compliance Statement (40 CFR §160.12): Included

Test Material: 2375.01 (Kleenex Brand Anti-Viral Tissue #2), white tissue with blue dots
Positive Control Material: Dinitrochlorobenzene (DNCB)

Species: Hartley guinea pigs
Weight: Males: 318-358 g, Females: 291-344 g
Age: Approximately 4 weeks
Source: Elm Hill Breeding Labs, Inc., Chelmsford, MA

Method: Buehler

Summary:

1. **This product is not a dermal sensitizer.**
2. **Classification:** Acceptable

Procedure (Deviation From §81-6, 870.2600): No deviations were noted.

Procedure: For the induction, a 20 mm x 20 mm section of the test material moistened with 0.1 mL of distilled water was applied to the clipped left shoulder area (blue dots against dosing area) under occlusion for six hours once each week for three weeks to 10 males and 10 females. Fourteen days after the last induction exposure, the animals were challenged with the test material using the same procedure as the induction under occlusion at naive sites for 6 hours. A naive control group (5 males and 5 females) was treated with the test material at challenge only. Reactions were scored 24 and 48 hours post exposure.

Results: No reaction was noted on any test animal after induction and challenge. The naive control animals had no reaction after challenge. An historical positive control study was not included with the original study report, but one was later cited (MRID 455757-09) and a copy Faxed to Product Science Branch at EPA. Dinitrochlorobenzene was the positive control substance; the results were appropriate.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

November 18, 2002

MEMORANDUM:

Subject: Efficacy Review for EPA Reg. No.: 9402-RN,"Kleenex® Brand Anti-Viral* Tissue #2"
DP Barcode: D284618
Case No: 072433

From: Emily Mitchell, M.S., Team Leader Emily Mitchell 11/18/02
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

To: Adam Heyward PM34/Drusilla Copeland
Regulatory Management Branch II
Antimicrobials Division (7510C)

Applicant: Kimberly-Clark Corporation
2100 Winchester Road
Neenah, WI 54957

Formulation From Label:

Active Ingredient(s)	% by wt.
Citric Acid	7.51%
Sodium Lauryl Sulfate	2.02%
Inert Ingredient(s)	90.47%
Total	100.00%

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I BACKGROUND

The product, Kleenex Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-RN), is a new "end-use" product. The applicant requested to register this virucidal facial tissue for use in hospitals, schools, churches, day care facilities, and physicians' offices. The environmental "surface" on which the product is intended to be active is the tissue itself. All laboratory studies were conducted at Hill Top Research, Inc., located at Main and Mill Streets in Miamiville, Ohio 45147.

This data package contained EPA Form 8570-4 (Confidential Statement of Formula), five laboratory studies (MRID Nos. 457138-11 through 457138-15), Statements of No Data Confidentiality Claims for all five laboratory studies, one confidential consumer survey study (MRID No. 457229-01), and the proposed label.

II USE DIRECTIONS

No specific directions for use (including the surface to be disinfected) are provided in the label section "Directions for Use." The proposed label directions state:

"Use to help prevent the spread of viruses*."
"Complete inactivation of viruses* within 15 minutes after contact."
"Dispose of used tissues in a normal fashion. Do not reuse empty container."

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Impregnated Towelettes for Hard Surface Disinfection – Single-Use Towelette

The complete product, as offered for sale, should be tested according to directions for use to ensure effectiveness in disinfecting hard surfaces. Basic efficacy data requirements in DIS/TSS-1 are required. Additionally, a modification of the AOAC Germicidal Spray Products Test should be employed, using one towelette to wipe the surface of each glass slide carrier, subculturing the slides, expressing the liquid from the used towelette, and subculturing the expressed liquid. Sterile gloves should be used to handle the towelette, and the towelette should be rotated between each wipe so as to expose a maximum amount of towelette surface area. Supplemental recommendations in DIS/TSS-2 should be met, and data reporting requirements of DIS/TSS-3 should be met. These standards are provided in "Efficacy Data Requirements: Pre-Saturated or Impregnated Towelettes for Hard Surface Disinfection."

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Disinfectants for Use on Hard Surfaces in Hospital or Medical Environments

The effectiveness of disinfectants for use on hard surfaces in hospital or medical environments must be substantiated by data derived using the AOAC Use-Dilution Method (for water soluble powders and liquid products) or the AOAC Germicidal Spray

Products Test (for spray products). Sixty carriers must be tested with each of 3 product samples, representing 3 different batches, one of which is at least 60 days old, against *Salmonella choleraesuis* (ATCC 10708), *Staphylococcus aureus* (ATCC 6538), and *Pseudomonas aeruginosa* (ATCC 15442). To support products labeled as "disinfectants," killing on 59 out of 60 carriers is required to provide effectiveness at the 95% confidence level. The above Agency standards are presented in DIS/TSS-1.

Virucides

The effectiveness of virucides against specific viruses must be supported by efficacy data that simulates, to the extent possible in the laboratory, the conditions under which the product is intended to be used. Carrier methods that are modifications of either the AOAC Use-Dilution Method (for liquid disinfectants) or the AOAC Germicidal Spray Products Test (for spray disinfectants) must be used in developing data for virucides intended for use upon dry inanimate, environmental surfaces (e.g., floors, tables, cleaned dried medical instruments). To simulate in-use conditions, the specific virus to be treated must be inoculated onto hard surfaces, allowed to dry, and then treated with the product according to the directions for use on the product label. One surface for each of two different batches of disinfectant must be tested against a recoverable virus titer of at least 10^4 from the test surface for a specified exposure period at room temperature. Then, the virus must be assayed by an appropriate virological technique, four replicates per dilution. The calculated viral titers must be reported with the test results. For the data to be considered acceptable, results must demonstrate complete inactivation of the virus at all dilutions. When cytotoxicity is evident, at least a 3-log reduction in titer must be demonstrated beyond the cytotoxic level. These Agency standards are presented in DIS/TSS-7.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 457138-11 "Virucidal Efficacy of Facial Tissue For Treated and Untreated Tissue Against Rhinovirus 1A, ATCC VR-1364" for Kleenex Brand Anti-Viral Tissue #2, by Kathleen A. Baxter. Study conducted at Hill Top Research, Inc. Study completion date – June 13, 2002.

This study was conducted against Rhinovirus 1A (ATCC VR-1364) using WI-38 cells (source not identified) as the host system. The study protocol followed a modification of ASTM Method E 1053-97, Standard Test Method for Efficacy of Virucidal Agents Intended for Inanimate Environmental Surfaces; a major modification

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was the use of 1-inch-square "disks" of tissue as the carrier in lieu of glass slides. The carriers were inoculated with undried virus (presence of organic soil load not indicated), and held for the indicated contact time. Three (3) lots of product were tested (Lot Nos. 3-7-02-4A, 3-7-02-4B, 3-7-02-4C (60 Day Stability Sample)) and compared against untreated tissue control disks (Lot No. 3-7-02-4D). Two disks punched out of individual tissue sheets prior to inoculation with test virus were placed side by side in a sterile 60 mm glass Petri plate in a laminar flow hood at 24±3°C. Each disk was inoculated with 100 µL of test virus distributed uniformly in a spiral fashion from the center of the disk. After 15 minutes exposure at 24±3°C, the product was neutralized by flooding with 5.0 mL of neutralizer (bovine serum albumin/HEPES buffer/sodium hydroxide solution). Contents of the Petri plate were transferred to a test tube and vortexed 30-40 seconds. Ten-fold serial dilutions (diluent not specified) were prepared and WI-38 cells were inoculated according to current Hill Top Research SOP 11-DISF-20-0028. The cell plates were incubated at 33±1°C for 3 days ± 4 hours in 5±1 CO_2. The cells were examined for unspecified cytopathic effect. Controls included virus controls, neutralizer effectiveness, and cytotoxicity. Viral and toxicity titers were calculated by the method of Reed and Muench (1938).

2. MRID 457138-12 "Virucidal Efficacy of Facial Tissue For Treated and Untreated Tissue Against Rhinovirus 2, ATCC VR-482" for Kleenex Brand Anti-Viral Tissue #2, by Kathleen A. Baxter. Study conducted at Hill Top Research, Inc. Study completion date – June 13, 2002.

This study was conducted against Rhinovirus 2 (ATCC VR-482) using WI-38 cells (source not identified) as the host system. The study protocol followed a modification of ASTM Method E 1053-97, Standard Test Method for Efficacy of Virucidal Agents Intended for Inanimate Environmental Surfaces; a major modification was the use of 1-inch-square "disks" of tissue as the carrier in lieu of glass slides. The carriers were inoculated with undried virus (presence of organic soil load not indicated), and held for the indicated contact time. Three (3) lots of product were tested (Lot Nos. 3-7-02-4A, 3-7-02-4B, 3-7-02-4C (60 Day Stability Sample)) and compared against untreated tissue control disks (Lot No. 3-7-02-4D). Two disks punched out of individual tissue sheets prior to inoculation with test virus were placed side by side in a sterile 60 mm glass Petri plate in a laminar flow hood at 24±3°C. Each disk was inoculated with 100 µL of test virus distributed uniformly in a spiral fashion from the center of the disk. After 15 minutes exposure at 24±3°C, the product was neutralized by flooding with 5.0 mL of neutralizer (bovine serum albumin/HEPES buffer/sodium hydroxide solution). Contents of the Petri plate were transferred to a test tube and vortexed 30-40 seconds. Ten-fold serial dilutions (diluent not specified) were prepared and WI-38 cells were inoculated according to current Hill Top Research SOP 11-DISF-20-0028. The plates were incubated at 33±1°C for 3 days ± 4 hours in 5±1 CO_2. The cells were examined for unspecified cytopathic effect. Controls included virus controls.

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Note: The MRID referenced a neutralizer effectiveness study conducted under HTR Study No. 02-120089-106 using the same cell line (i.e., WI-38 cells) and the same product. This HTR study is MRID No. 457138-11 (see above).

3. MRID 457138-13 "Virucidal Efficacy of Facial Tissue For Treated and Untreated Tissue Against Influenza A, ATCC VR-1469" for Kleenex Brand Anti-Viral Tissue #2, by Kathleen A. Baxter. Study conducted at Hill Top Research, Inc. Study completion date – June 12, 2002.

This study was conducted against Influenza A (ATCC VR-1469) using MDCK cells (source not identified) as the host system. The study protocol followed a modification of ASTM Method E 1053-97, Standard Test Method for Efficacy of Virucidal Agents Intended for Inanimate Environmental Surfaces; a major modification was the use of 1-inch-square "disks" of tissue as the carrier in lieu of glass slides. The carriers were inoculated with undried virus (presence of organic soil load not indicated), and held for the indicated contact time. Three (3) lots of product were tested (Lot Nos. 3-7-02-4A, 3-7-02-4B, 3-7-02-4C (60 Day Stability Sample)) and compared against untreated tissue control disks (Lot No. 3-7-02-4D). Two disks punched out of individual tissue sheets prior to inoculation with test virus were placed side by side in a sterile 60 mm glass Petri plate in a laminar flow hood at 24±3°C. Each disk was inoculated with 100 µL of test virus distributed uniformly in a spiral fashion from the center of the disk. After 15 minutes exposure at 24±3°C, the product was neutralized by flooding with 5.0 mL of neutralizer (bovine serum albumin/HEPES buffer/sodium hydroxide solution). Contents of the Petri plate were transferred to a test tube and vortexed 30-40 seconds. Ten-fold serial dilutions (diluent not specified) were prepared and MDCK cells were inoculated according to current Hill Top Research SOP 11-DISF-20-0037. The plates were incubated at 33±1°C for 7±1 days in 5±1% CO_2. The cells were examined for unspecified cytopathic effect. After 7±1 days, a hemagglutination assay was conducted. Controls included virus controls, neutralizer effectiveness, and cytotoxicity. Viral and toxicity titers were calculated by the method of Reed and Muench (1938).

4. MRID 457138-14 "Virucidal Efficacy of Facial Tissue For Treated and Untreated Tissue Against Influenza B, CDC ID# 2001701156" for Kleenex Brand Anti-Viral Tissue #2, by Kathleen A. Baxter. Study conducted at Hill Top Research, Inc. Study completion date – June 12, 2002.

This study was conducted against Influenza B (CDC ID# 2001701156) using MDCK cells (source not identified) as the host system. The study protocol followed a modification of ASTM Method E 1053-97, Standard Test Method for Efficacy of Virucidal Agents Intended for Inanimate Environmental Surfaces; a major modification was the use of 1-inch-square "disks" of tissue as the carrier in lieu of glass slides. The carriers were inoculated with undried virus (presence of organic soil load not indicated), and held for the indicated contact time. Three (3) lots of product were tested (Lot Nos. 3-7-02-4A, 3-7-02-4B, 3-7-02-4C (60 Day Stability Sample)) and compared against

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untreated tissue control disks (Lot No. 3-7-02-4D). Two disks punched out of individual tissue sheets prior to inoculation with test virus were placed side by side in a sterile 60 mm glass Petri plate in a laminar flow hood at 24±3°C. Each disk was inoculated with 100 µL of test virus distributed uniformly in a spiral fashion from the center of the disk. After 15 minutes exposure at 24±3°C, the product was neutralized by flooding with 5.0 mL of neutralizer (bovine serum albumin/HEPES buffer/sodium hydroxide solution). Contents of the Petri plate were transferred to a test tube and vortexed 30-40 seconds. Ten-fold serial dilutions (diluent not specified) were prepared and MDCK cells were inoculated according to current Hill Top Research SOP 11-DISF-20-0038.. The plates were incubated at 33°C for 7±1 days in 5±1% CO_2. The cells were examined for unspecified cytopathic effect. After 7±1 days, a hemagglutination assay was conducted. Controls included virus controls.

Note: The MRID referenced a neutralizer effectiveness study conducted under HTR Study No. 02-120048-106 using the same cell line (i.e., MDCK cells) and the same product. This HTR study is MRID No. 457138-13 (see above).

5. MRID 457138-15 "Virucidal Efficacy of Facial Tissue For Treated and Untreated Tissue Against Respiratory Syncytial Virus, ATCC VR-26" for Kleenex Brand Anti-Viral Tissue #2, by Kathleen A. Baxter. Study conducted at Hill Top Research, Inc. Study completion date – June 13, 2002.

This study was conducted against Respiratory Syncytial Virus (ATCC VR-26) using LLMK2 cells (source not identified) as the host system. The study protocol followed a modification of ASTM Method E 1053-97, Standard Test Method for Efficacy of Virucidal Agents Intended for Inanimate Environmental Surfaces; a major modification was the use of 1-inch-square "disks" of tissue as the carrier in lieu of glass slides. The carriers were inoculated with undried virus (presence of organic soil load not indicated), and held for the indicated contact time. Three (3) lots of product were tested (Lot Nos. 3-7-02-4A, 3-7-02-4B, 3-7-02-4C (60 Day Stability Sample)) and compared against untreated tissue control disks (Lot No. 3-7-02-4D). Two disks punched out of individual tissue sheets prior to inoculation with test virus were placed side by side in a sterile 60 mm glass Petri plate in a laminar flow hood at 24±3°C. Each disk was inoculated with 100 µL of test virus distributed uniformly in a spiral fashion from the center of the disk. After 15 minutes exposure at 24±3°C, the product was neutralized by flooding with 5.0 mL of neutralizer (bovine serum albumin/HEPES buffer/sodium hydroxide solution). Contents of the Petri plate were transferred to a test tube and vortexed 30-40 seconds. Ten-fold serial dilutions (diluent not specified) were prepared and LLMK2 cells were inoculated according to current Hill Top Research SOP 11-DISF-20-0041A. The plates were incubated at 37±1°C for 10 days ± 4 hours in 5±1% CO_2. The cells were examined for unspecified cytopathic effect. Controls included virus controls, neutralizer effectiveness, and cytotoxicity. Viral and toxicity titers were calculated by the method of Reed and Muench (1938).

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6. MRID 457229-01 "Consumer Survey: Facial Tissue Life Study, Project FACT (Flu and Cold Tissue)," Author, Completion Date, and Performing Laboratory Not Applicable

This study was conducted to obtain information about facial tissues. The applicant is claiming the nature of this study and its results as confidential. This 10-page document describes the study and presents the results. The applicant intends to use the information in developing a marketing strategy for the product, Kleenex Brand Anti-Viral Tissue #2.

V RESULTS

		Reduction of viral titer			
MRID Number	Organism	Lot No. 3-7-02-4A	Lot No. 3-7-02-4B	Lot No. 3-7-02-4C	Cytotoxicity
457138-11	Rhinovirus 1A	complete inactivation	complete inactivation	complete inactivation	No cytotoxicity observed
	Avg. titer control ($TCID_{50}$/0.1 mL)	4.2 log_{10}	4.2 log_{10}	3.7 log_{10}	
457138-12	Rhinovirus 2	complete inactivation	complete inactivation	complete inactivation	No cytotoxicity data provided
	Avg. titer control ($TCID_{50}$/0.1 mL)	3.6 log_{10}	3.6 log_{10}	3.6 log_{10}	
457138-13	Influenza A	complete inactivation	complete inactivation	complete inactivation	No cytotoxicity observed
	Avg. titer control ($TCID_{50}$/0.1 mL)	4.9 log_{10}	4.9 log_{10}	3.9 log_{10}	
457138-14	Influenza B	complete inactivation	complete inactivation	complete inactivation	No cytotoxicity data provided
	Avg. titer control ($TCID_{50}$/0.1 mL)	4.9 log_{10}	4.9 log_{10}	>4.8 log_{10}	
457138-15	Respiratory Syncytial Virus	complete inactivation	complete inactivation	complete inactivation	No cytotoxicity observed
	Avg. titer control ($TCID_{50}$/0.1 mL)	5.5 log_{10}	5.5 log_{10}	4.9 log_{10}	

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VI CONCLUSIONS

1. The submitted efficacy data (MRID Nos. 457138-11 and 457138-13 through -15) appear to support the use of the product, Kleenex Brand Anti-Viral Tissue #2, as a virucide when tested against the following microorganisms for a contact time of 15 minutes:

Influenza A
Influenza B
Respiratory Syncytial Virus
Rhinovirus 1A

Complete inactivation was observed for all dilutions assayed. [The laboratory used a >3-log reduction in titer as the performance standard.] No cytotoxicity was observed in studies against Rhinovirus 1A, Influenza A, or Respiratory Syncytial Virus. Cytotoxicity data were not provided for the study Influenza B (MRID No. 457138-14); rather the MRID referenced cytotoxicity data that had been developed for the same cell line and the same product in support of another study (MRID No. 457138-13). The Agency also notes that there was no specific description of the characteristics of the cytopathic effects produced by each of the test viruses in the cell monolayer – quantitation using cytopathic effect, which can be subjective, is less desirable than objective techniques such as immunofluorescence. Finally, DIS/TSS-7 indicates that the recoverable virus titer must be at least 10^4. One of three product lots tested against Rhinovirus 1A (MRID No. 457138-11) and Influenza A (MRID No. 457138-13) did not meet that quality control requirement. For virucidal efficacy claims, however, only two product lots need be tested.

2. The submitted efficacy data (MRID No. 457138-12) do not appear to support the use of the product, Kleenex Brand Anti-Viral Tissue #2, as a virucide when tested against Rhinovirus 2 for a contact time of 15 minutes. Although complete inactivation was observed for all dilutions assayed, the recoverable virus titer was not at least 10^4 for any of the product lots tested.

3. The Agency reviewed the confidential results of the consumer survey (MRID No. 457229-01) and found no reason to adjust the conclusion presented above.

VII RECOMMENDATIONS

Despite the favorable efficacy study results, the proposed label claims are not currently acceptable regarding the use of the product, Kleenex Brand Anti-Viral Tissue #2, as a virucide against Rhinovirus 1A and 2, Influenza A and B, and Respiratory Syncytial Virus for a contact time of 15 minutes. As noted previously, the study against Rhinovirus 2 did not meet the DIS/TSS-7 requirement that the recoverable virus titer must be at least 10^4. Furthermore, the Agency standards for impregnated towelettes for hard surface disinfection do not apply to this impregnated facial tissue.

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- EPA's standards for environmental surfaces are hard, inanimate surfaces, either porous or non-porous. Based on the study methodology, the tissue itself (as opposed to a human face or nose) is the surface of interest. A facial tissue is porous and is also soft.

- The product has not been registered as a disinfectant (i.e., successfully tested against bacteria *Salmonella choleraesuis* and *Staphylococcus aureus*, with or without *Pseudomonas aeruginosa*). Although three product lots (including a 60-day-old lot) were tested in the virucidal studies provided in this data package, the Agency will register a product tested merely as a virucide without having met basic disinfectant claims in DIS/TSS-1.

- An organic soil load was not mentioned in any of the studies. Although viral inoculum is frequently accompanied by some naturally-occurring organic soil (e.g., serum), in actual use, the product would be challenged with 100 percent organic soil load (e.g., nasal mucus, eye discharge, phlegm, and/or sputum). The applicant must provide data about the nature and concentration of the organic soil load challenge (if any) employed in these studies.

- The proposed label claims indicate that the product can be used in hospital settings. A mere virucide can not make that claim. The applicant has not provided efficacy data against *Pseudomonas aeruginosa*, which is an Agency requirement for a hospital disinfectant claim.

- The claim for 15 minutes is questionable. A tissue is usually disposed of in 1 or 2 minutes after use. A more appropriate contact time would be 30 seconds.

- What are the benefits of this product?

PM Note: As noted earlier, directions for use, a requirement for a pesticide, are not clear. Consumers, however, are likely to know how to use a facial tissue. PSB is not certain what should be included in the directions for use, but at a minimum, the probable source of the viral load (e.g., nose blowing) and the surface being treated (the tissue itself) need to be mentioned. In addition, the current instruction "Dispose of used tissues in a normal fashion" might be better phrased as "Dispose of used tissues promptly."

Other proposed label wording issues:

- Other questionable phrases [see page 2 of the label], implying "newness," include: "NOW with" and "Introducing a revolution in facial tissues."

- The PM should review the repeated use of percent kill (99.9%) on the proposed label [see page 2 of the label]; although accurate, this is not the Agency's virucidal performance standard in the absence of cytotoxicity.

- The proposed label repeatedly indicates the product's ability to "kill 99.9% of virus*" [see page 2 of the label]; this is an incomplete phrase and is not acceptable. However, "kill virus* on the used facial tissue in 15 minutes" may be more acceptable.
- Optional terms suggested on the proposed label [see page 3 of the label] include "clinically" testing efficacy; only non-clinical (i.e., no human subject) efficacy study reports were provided with this data package.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES
Antimicrobials Division

November 8, 2002

SUBJECT: PRODUCT CHEMISTRY REVIEW OF:

Kleenex® Brand Anti-Viral Tissue #2

DP Barcode:D284616 **Reg. No. Or File Symbol: 9402-RN**
Manufacturing-use [X] OR **End-use Product []**

TO: Adam Heyward / Drusilla Copeland
PM Team 34

FROM: Juan F. Negron, Chemist
Product Science Branch, CT Team
Antimicrobial Division (7510C)

THRU: Karen P. Hicks, CT Team Leader
Product Science Branch
Antimicrobial Division (7510C)

11-19-02

THRU: Michele E. Wingfield, Chief
Product Science Branch
Antimicrobial Division (7510C)

APPLICANT: Kimberly - Clark Corp

Product Formulation **Active Ingredient(s)**	**% by wt.**
Citric acid	7.51
Sodium lauryl sulfate	2.02

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I. **BACKGROUND:** The registrant has withdrawn (January 2002) the registration application for Kleenex® Brand Anti-Viral Tissue (EPA Reg. No. 9402-I) and submitted the required materials for registration of Kleenex® Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-RN). In a letter dated 7/5/2002, the registrant indicates that citric acid is widely used in numerous foods and sodium lauryl sulfate is used as surfactant in shampoos, skin cleaners, and bath and shower products. The letter also indicates that the company has marketed a silicone treated tissue - Kleenex® UltraSoft Facial Tissue that contains "similar inert ingredients at similar concentrations as those used in Kleenex® Brand Anti-Viral tissue #2."

FINDINGS

1. The registrant has submitted the following: Confidential Statements of Formula (CSF) dated 7/5/02 & 10/14/02; flu and cold tissue spike recovery data, dated 10/4/02; sodium lauryl sulfate and citric acid methods; Data Matrix, EPA Form 8570-35 dated 7/5/02; letters dated 7/5/02 and 10/14/02; Volume 1, Product Identity and Composition, Description of Beginning Materials, Manufacturing Process, Discussion of Potential Impurity Formation, MRID # 457138-01; Volume 2, Analysis and Certification of Product Ingredients and Analytical Method to Verify Certified Limits, MRID # 457138-02; Volume 3, Verification of Active Ingredients, Storage stability and Weight of Dry Tissue; Volume 4, Storage stability and Weight of Dry Tissue, MRID # 457138-04; the label.

2. The CSF, dated 7/5/02, is obsolete.

3. The CSF, dated 10/14/02, is the revised CSF.

4. The registrant submitted a pre- & post-reaction CSF.

5. The pre-reaction CSF is a virucidal coating containing an aqueous solution of citric acid and sodium lauryl sulfate (SLS) in [redacted]

6. The SLS purity has been reported in the pre-reaction CSF. However, the post-reaction CSF does not report the purity.

7. The [redacted] is removed in the post-reaction CSF. The mixed dry tissue contains Citric acid and sodium lauryl sulfate. The [redacted] are added during the post-reaction.

8. The registrant is requesting a wider range for the AI and its inerts, and they are acceptable.

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9. The following inerts have not been cleared by the Agency:
[redacted]

10. The registrant has unregistered sources.

11. The manufacturing process that describes the viral coating made from the active ingredients is shown in volume one (MRID #457138-01) page 17,18,19,20 & 23 of 25.

12. No physical/chemical characteristics were reported except for the information on the CSF. The data matrix states "not applicable" on the "Generic Data Matrix." Therefore, the "End-use Data Matrix" reported "Not Applicable."

13. No CAS Nos. were provided for the inerts [redacted] and [redacted] on the CSF. The study (MRID 45713801, page 4) indicates that the CAS Nos. "will be provided directly to the Agency by the supplier." A MSDS of [redacted] is included in the study. No MSDS for [redacted] was found in the study.

14. The registrant states that the certified limits of the [redacted] falls within the recommended range [redacted] However, the MRID 45713802 states that the certified limits for the [redacted] range from [redacted] of the nominal concentration. Calculation shows that the upper limit is actually [redacted] and the lower limit is [redacted] of the nominal concentration.

15. The registrant had submitted an amendment for the analytical enforcement method, and a "flu and Cold Tissue Spike Recovery Data"that shows how the method performs when assaying the AIs (see letter dated 10/14/02) from the tissue.

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RECOMMENDATIONS

1. The CSF, dated 10/14/02, is not acceptable. The CSF consisted of two CSFs for a pre- & post-reaction CSF.

2. The registrant should clarify that the post-reaction used [redacted] when in the pre-reaction they produce a total weight of [redacted]

3. The registrant must type " List 4" under the column 12 for the AI citric acid.

4. The registrant should type "pre-reaction" in addition to the product name in box 3 in the pre-reaction CSF.

5. The registrant should type "post-reaction" in addition to the product name in box 3 in the post-reaction CSF.

6. The registrant needs to provide the CAS numbers for [redacted] and [redacted] on the CSF.

7. The registrant should report the purity of SLS in the post-reaction CSF.

8. The [redacted] and [redacted] do not have clearance as inerts. The registrant must request from the suppliers the following:
   - The chemical names of all the components in the ingredient
   - The CAS numbers of all the components
   - The percentage amounts of each of the components in the ingredient (Total must equal 100%, although ranges are acceptable.)

Conclusion

The CSF, dated 10/14/02, is not acceptable. The CSF and the label have the same nominal. The registrant must address all requirements, recommendations, and concerns mentioned above. The SLS is under the title "21 CFR 178.1010 Sanitizing solutions", and the guideline states that the compound may be used safely on food-processing equipment and utensils, and on other food-contact articles, except milk containers or equipment, as it specifies in the section. The registrant must clear the inerts, [redacted]

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IV. PRODUCT CHEMISTRY REVIEW:

9. CONFIDENTIAL STATEMENT OF FORMULA (CSF):

1a. Type of manufacturing process and source active ingredient registration
- Non-integrated formulation system (i.e., all TGAI in product are registered) [x]
- Integrated production system [ ]
- if "ME-TOO," specify EPA Reg. # of existing product: _____

TABLE 1. Product Identity, Composition, and Certified Limits

PRODUCT NAME: Kleenex® Brand Anti-Viral Tissue #2 EPA Reg. #: 9402-RN							
Ingredient name (% purity)	CAS Reg. #	PC Code	EPA Reg. #	Ingredient concentration in product, % w/w			Purpose in formulation
				Nominal	Upper limit	Lower limit	
Citric acid	77-92-9	021801		7.51	9.11	6.00	Active
Sodium lauryl sulfate	151-21-3	079011		2.02	2.44	1.61	Active
[redacted]							

1b. Clearance of inerts for non-food or food use:
Cleared for food use under 40 CFR §180.1001: Yes [ ] No [x] NA [ ]

1c. The chemical identity, composition (including that for the TGAI), density, pH, and flammability on the CSF are consistent with guidelines in OPPTS Series 830, Part A and OPPTS 830.7300, 830.7000, and 830.6315 respectively: Yes [x]* No [ ]
*Note: Not applicable for pH and flammability as indicated on the "End Use Data Matrix" in the submission.

1d. Nominal Concentrations and Certified Limits for active ingredients are:
Acceptable [x] Not acceptable [ ]

1e. Nominal Concentrations and Certified Limits for inert ingredients are:
Acceptable [x] Not acceptable [ ] Not applicable [ ]

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1f. For products produced by an integrated formulation system:
- All impurities of toxicological significance have an Upper Certified Limit?
  Yes [ ] No [ ] Not applicable [x]
- All impurities of ≥ 0.1% in the product have been identified?
  Yes [ ] No [ ] Not applicable [x]

10. PRODUCT LABEL:

2a. The active ingredients statement (chemical IDs and Nominal Concentrations) on the label is consistent with the CSF? Yes [x] No [ ]

2b. The product contains one of the following:
- 10% or more of a petroleum distillate: Yes [ ] No [x]
- 1.0% or more of methyl alcohol: Yes [ ] No [x]
- sodium nitrite at any level: Yes [ ] No [x]
- a toxic List 1 inert at any level: Yes [ ] No [x]
- arsenic in any form: Yes [ ] No [x]

2c. If Yes to any of the above, does the inert ingredients statement contain a footnote indicating this? Yes [ ] No [ ] Not applicable [x]

2d. The appropriate warning statement regarding flammability or explosive characteristics of the product are listed on the label? Yes [ ] No [ ] Not applicable [x]

2e. The storage and disposal instructions for the pesticide and container are in compliance with PR Notice 84-1 for household use products or PR Notice 83-3 for all other uses?
Yes [x] No [ ]

2f. Does the product require an expiration date at which time the Nominal Concentration falls below the Lower Certified Limit (based on the one year storage stability data or other information)? Yes [ ] No [ ]*
*Note: Unknown, storage stability study is in progress.

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11. OPPTS SERIES §830 GUIDELINES:

TABLE 2. Product Chemistry Series 830, Part A

OPPTS Guideline	Acceptance of Information*	MRID No. and other Source
830.1550 Chemical ID[1]	A	45713801
830.1600 Description of Materials	A	45713801
830.1620 Production Process[2]	NA	
830.1650 Formulation Process[3]	U	45713801
830.1670 Discussion of Impurities[4]	A	45713801
830.1700 Preliminary Analysis[5]	A•	45713802
830.1750 Certified Limits[6]	A	45713802
830.1800 Analytical Method for AIs	A	45713803

*Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; NR= not required, G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

[1]See Table 1 of Product Chemistry Review for additional information.

[2]For MP or EP products manufactured by an integrated production system.

[3]For products manufactured by a non-integrated system (i.e., using a registered TGAI or MP).

[4]May be waived unless actual/possible impurities are of toxicological concern.

[5]Five batch analysis required for products produced by an integrated production system.

[6]If different from standard Certified Limits recommended in 40 CFR 158.175, discussed under "Findings" of the Product Chemistry Review.

• Four batches of citric acid, five batches of sodium lauryl sulfate, and three samples of the end-use product were analyzed.

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TABLE 3. Product Chemistry Series 830, Part B

Physical/Chemical Properties		Acceptance of data*	Value or qualitative description**	MRID No. and other source
830.6302	Color		Not applicable[1]	
830.6303	Physical State	A	Silicone coated tissue	45713801
830.6304	Odor		Not applicable[1]	
830.6314	Oxidation/Reduction		Not applicable[1]	
830.6315	Flammability/Flash Pt		Not applicable[1]	CSF
830.6316	Explodability		Not applicable[1]	
830.6317	Storage Stability		In progress	45713803, 45713804
830.6320	Corrosion Character		Not applicable[1]	
830.7000	pH		Not applicable[1]	
830.7100	Viscosity		Not applicable[1]	
830.7300	Density/sp. gravity	A	26.77 lbs/2880 ft^2	CSF

*Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; NR= Not required G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

[1] As reported on "End Use Data Matrix"

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DATA EVALUATION RECORD

CITRIC ACID
SODIUM LAURYL SULFATE
(KLEENEX® BRAND ANTI-VIRAL TISSUE #2)

STUDY TYPES: **Product Identity and Composition (OPPTS 830.1550)**
Description of Beginning Materials (OPPTS 830.1600)
Description of Formulation Process (OPPTS 830.1650)
Discussion of Formation of Impurities (OPPTS 830.1670)
Preliminary Analysis (OPPTS 830.1700)
Certified Limits (OPPTS 830.1750)
Enforcement Analytical Method (OPPTS 830.1800)
Physical and Chemical Characteristics (OPPTS 830.6302-830.7950)
MRIDs 45713801, 45713802, 45713803, and 45713804

Prepared for
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
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Quality Assurance:
Lee Ann Wilson, M.A.

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Date: SEP 0 9 2002

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES
Antimicrobials Division

September 9, 2002

SUBJECT:	PRODUCT CHEMISTRY REVIEW OF: Kleenex® Brand Anti-Viral Tissue #2
DP Barcode:	D284616
Reg. No. or File Symbol	9402-RN

TGAI/Manufacturing-use Product [ ] OR End-use Product [x]

TO:	(Team leader/Regulator) PM Team (#)
FROM:	(Reviewer), Chemist Product Science Branch, CT Team Antimicrobials Division (7510C)
THRU::	Karen P. Hicks, CT Team Leader Product Science Branch Antimicrobials Division (7510C)
THRU:	Michele E. Wingfield, Chief Product Science Branch Antimicrobials Division (7510C)

Product Formulation

Active Ingredients	**% by wt.**
Citric acid	7.51%
Sodium lauryl sulfate	2.0%

I. BACKGROUND: The registrant has withdrawn (January 2002) the registration application for Kleenex® Brand Anti-Viral Tissue (EPA Reg. No. 9402-I) and submitted the required materials for registration of Kleenex® Brand Anti-Viral Tissue #2 (EPA Reg. No. 9402-RN). In a letter dated 7/5/2002, the registrant indicates that citric acid is widely used in numerous foods and sodium lauryl sulfate is used as surfactant in shampoos, skin cleaners, and bath and shower products. The letter also indicates that the company has marketed a silicone treated tissue - Kleenex® UltraSoft Facial Tissue that contains "similar inert ingredients at similar concentrations as those used in Kleenex® Brand Anti-Viral tissue #2."

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II. FINDINGS:

1. The manufacturing process did not describe how the viral coating was made from the active ingredients.
2. No physical/chemical characteristics was reported except the information on the CSF. The data matrix states "not applicable".
3. No CAS Nos. were provided for the inerts [redacted] on the CSF. The study (MRID 45713801, page 4) indicates that the CAS Nos. "will be provided directly to the Agency by the supplier." A MSDS of [redacted] is included in the study. No MSDS for [redacted] was found in the study.
4. No PC codes were found for the inerts [redacted] and [redacted]
5. The certified upper and lower limits of all ingredients on the CSF are outside the recommended range. A "note to reviewer"in the submission explains the wide limits for the active ingredients and the inert [redacted] It also states that the limits of the [redacted] falls within the recommended range [redacted] This is incorrect, the upper limit is actually [redacted] and the lower limit is [redacted] of the nominal concentration. In fact, MRID 45713802 states that the certified limits for the [redacted] range from [redacted] of the nominal concentration.

III. RECOMMENDATIONS:

1. The applicant needs to provide more details of the manufacturing process.
2. The applicant needs to provide CAS Nos. and PC codes for [redacted] and [redacted] on the CSF.
3. The applicant needs to submit the one-year storage stability study results when they are completed.
4. If the storage stability study indicates an expiration date is needed, the applicant needs to add this to the product label.
5. The applicant needs to explain why physical and chemical characteristics are not applicable.

IV. PRODUCT CHEMISTRY REVIEW:

6. CONFIDENTIAL STATEMENT OF FORMULA (CSF):

1a. Type of manufacturing process and source active ingredient registration
- Non-integrated formulation system (i.e., all TGAI in product are registered) [x]
- Integrated production system [ ]
- if "ME-TOO," specify EPA Reg. # of existing product: _____

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TABLE 1. Product Identity, Composition, and Certified Limits

PRODUCT NAME: Kleenex® Brand Anti-Viral Tissue #2 EPA Reg. #: 9402-RN							
Ingredient name (% purity)	CAS Reg. #	PC Code	EPA Reg. #	Ingredient concentration in product, % w/w			Purpose in formulation
				Nominal	Upper limit	Lower limit	
Citric acid	77-92-9	021801		7.51	9.11	6.00	Active
Sodium lauryl sulfate	151-21-3	079011		2.02	2.44	1.61	Active

[redacted]

1b. Clearance of inerts for non-food or food use:
Cleared for food use under 40 CFR §180.1001: Yes [ ] No [x] NA [ ]

1c. The chemical identity, composition (including that for the TGAI), density, pH, and flammability on the CSF are consistent with guidelines in OPPTS Series 830, Part A and OPPTS 830.7300, 830.7000, and 830.6315 respectively: Yes [x]* No [ ]
*Note: Not applicable for pH and flammability as indicated on the "End Use Data Matrix" in the submission.

1d. Nominal Concentrations and Certified Limits for active ingredients are:
Acceptable [x] Not acceptable [ ]

1e. Nominal Concentrations and Certified Limits for inert ingredients are:
Acceptable [x] Not acceptable [ ] Not applicable [ ]

1f. For products produced by an integrated formulation system:
- All impurities of toxicological significance have an Upper Certified Limit?
  Yes [ ] No [ ] Not applicable [x]
- All impurities of ≥ 0.1% in the product have been identified?
  Yes [ ] No [ ] Not applicable [x]

7. PRODUCT LABEL:

2a. The active ingredients statement (chemical IDs and Nominal Concentrations) on the label is consistent with the CSF? Yes [x] No [ ]

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2b. The product contains one of the following:

- 10% or more of a petroleum distillate: Yes [ ] No [x]
- 1.0% or more of methyl alcohol: Yes [ ] No [x]
- sodium nitrite at any level: Yes [ ] No [x]
- a toxic List 1 inert at any level: Yes [ ] No [x]
- arsenic in any form: Yes [ ] No [x]

2c. If Yes to any of the above, does the inert ingredients statement contain a footnote indicating this? Yes [ ] No [ ] Not applicable [x]

2d. The appropriate warning statement regarding flammability or explosive characteristics of the product are listed on the label? Yes [ ] No [ ] Not applicable [x]

2e. The storage and disposal instructions for the pesticide and container are in compliance with PR Notice 84-1 for household use products or PR Notice 83-3 for all other uses? Yes [x] No [ ]

2f. Does the product require an expiration date at which time the Nominal Concentration falls below the Lower Certified Limit (based on the one year storage stability data or other information)? Yes [ ] No [ ]*

*Note: Unknown, storage stability study is in progress.

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8. OPPTS SERIES §830 GUIDELINES:

TABLE 2. Product Chemistry Series 830, Part A

OPPTS Guideline	Acceptance of Information*	MRID No. and other Source
830.1550 Chemical ID[1]	A	45713801
830.1600 Description of Materials	U	45713801
830.1620 Production Process[2]	NA	
830.1650 Formulation Process[3]	U	45713801
830.1670 Discussion of Impurities[4]	A	45713801
830.1700 Preliminary Analysis[5]	A*	45713802
830.1750 Certified Limits[6]	A	45713802
830.1800 Analytical Method for AIs	A	45713803

*Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; NR= not required, G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

[1]See Table 1 of Product Chemistry Review for additional information.

[2]For MP or EP products manufactured by an integrated production system.

[3]For products manufactured by a non-integrated system (i.e., using a registered TGAI or MP).

[4]May be waived unless actual/possible impurities are of toxicological concern.

[5]Five batch analysis required for products produced by an integrated production system.

[6]If different from standard Certified Limits recommended in 40 CFR 158.175, discussed under "Findings" of the Product Chemistry Review.

* Four batches of citric acid, five batches of sodium lauryl sulfate, and three samples of the end-use product were analyzed.

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TABLE 3. Product Chemistry Series 830, Part B

Physical/Chemical Properties		Acceptance of data*	Value or qualitative description**	MRID No. and other source
830.6302	Color		Not applicable[4]	
830.6303	Physical State	A	Silicone coated tissue	45713801
830.6304	Odor		Not applicable[4]	
830.6314	Oxidation/Reduction		Not applicable[4]	
830.6315	Flammability/Flash Pt		Not applicable[4]	CSF
830.6316	Explodability		Not applicable[4]	
830.6317	Storage Stability		In progress	45713803, 45713804
830.6320	Corrosion Character		Not applicable[4]	
830.7000	pH		Not applicable[4]	
830.7100	Viscosity		Not applicable[4]	
830.7300	Density/sp. gravity	A	26.77 lbs/2880 ft^2	CSF

*Explanation: A=acceptable; N=not acceptable; NA=technically not applicable; NR= Not required G=data gap; U=requires upgrading; W=waived; E=EPA estimate.

[4] As reported on "End Use Data Matrix"

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EPA Reg # 9402-10

Page____ is not included in this copy.

Pages 201 through 207 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

✓ The document is a duplicate of page(s) 194-200.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

EPA Reg #9402-10

Page 208 is not included in this copy.

Pages ____ through ____ are not included.

The material not included contains the following type of information:

- ✓ Identity of product inert ingredients.
- ____ Identity of product impurities.
- ✓ Description of the product manufacturing process.
- ____ Description of quality control procedures.
- ____ Identity of the source of product ingredients.
- ____ Sales or other commercial/financial information.
- ____ A draft product label.
- ____ The product confidential statement of formula.
- ____ Information about a pending registration action.
- ____ FIFRA registration data.
- ____ The document is a duplicate of page(s) _____.
- ____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

LEWIS &
HARRISON
Consultants In Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

October 14, 2002

Juan Negron, Chemist
Product Registration Branch
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, CM#2
Arlington, VA 22202

re: **Kleenex® Brand Anti-Viral Tissue #2**
EPA File Symbol No. 9402-RN
Registrant: Kimberly-Clark Corporation
Product Chemistry Issues

Dear Juan:

I am writing you as a follow-up to our telephone conference call on Wednesday, October 2nd regarding certain product chemistry issues you raised concerning Kleenex® Brand Anti-Viral Tissue #2. The specific issues and Kimberly-Clark's responses are detailed below:

Issue #1

Regard Study Volume #3, MRID No. 45713803 (and Study Volume #4, MRID No. 45713804) the following information/clarification should be provided:

- Explain how the bromophenol blue (item 2.2.5 on page 23 of 31) is prepared and whether the percentage is weight volume or volume/volume.
- Identify catalog numbers for the laboratory glassware.
- Explain what the number "10" signifies in the equation under item 8.4 on page 27 of 31.

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- Clarify the use of the "blank titer" in the equation under item 7.0 on page 24 of 31.
- Explain in more detail the sample preparation procedure.
- Explain how the percentages of citric acid and sodium lauryl sulfate are calculated.

Kimberly-Clark Response
The requested information on bromophenol blue is provided in the revised Standard Operating Procedure (SOP) No. 11.5.3, which is attached. The catalog numbers are also provided in the revised SOP in the Equipment section (item 3.0). The "10" in the equation in item 8.4 is the dilution factor and is now shown, in revised SOP No. 11.6.3, as DF . The use of the blank titer should not be an issue since the titration for sodium lauryl sulfate is a back titration and does not involve the use of a blank tissue. The sample preparation is described in more detail in SOP No. 11.6.3, item 6.0. The procedures to determine the percentages of citric acid and sodium lauryl sulfate in the treated tissue are provided in items 8.5 and 8.6 for SOP No. 11.6.3 and in item 7.2 for SOP No. 11.5.3.

Issue No. 2
Provide information from a spiking study that shows recoveries of citric acid and sodium lauryl sulfate from treated tissue.

Kimberly-Clark Response
A spiking study showing adequate recoveries is attached.

Issue No. 3
Provide a "pre-reaction" or "pre-loading" (onto the tissue) CSF that will account for the water in the sodium lauryl sulfate

Kimberly-Clark Response
The pre-reaction or pre-loading CSF for the virucidal coating is attached. Note that the water is lost during the drying of the tissue after the virucidal coating has been added.

Issue No. 4
Provide an explanation for the certified limits proposed on the finished product CSF.

Kimberly-Clark Response
The rationale for the expanded certified limits is attached. In addition, please note that a revised CSF for the finished product that identifies the actual percentage of citric acid that has been added is also enclosed.

(9-10)

Issue No. 5
Provide the CASRN's for the [redacted] and the [redacted]

Kimberly-Clark Response
It is our understanding that the supplier's of these substances has provided this information directly to the Agency.

Issue No. 6
Clarify the manufacturing process, in particular, how the virucidal coating is added.

Kimberly-Clark Response
As we discussed during our telephone conversation on October 2nd, the virucidal coating is added using a [redacted] This process is described on page 23 of 25 of the Confidential Appendix of Volume 1.

If you need any additional information, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark

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EPA Reg # 9402-10

Page____ is not included in this copy.

Pages 212 through 222 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

✓ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

July 23, 2002

Adam Heyward, Product Manager (34)
Regulatory Management Branch #2
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, Crystal Mall #2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
Applicant: Kimberly-Clark Corporation
EPA File Symbol Number: 9402-
Data Transmittal Letter for Resubmission of Study Supporting
FIFRA Section 3 Registration of a New End-Use Product

Dear Mr. Heyward:

On behalf of Kimberly-Clark Corporation, I am resubmitting three (3) copies of the following study:

- Volume 1 of 1
  Consumer Survey: Facial Life Study, Project FACT (Flu and Cold Tissue)
  MRID#

Please note that the study now includes the required "Supplemental Claim of Data Confidentiality".

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark Corporation

N/FT

LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
telephone 202.393.3903
fax 202.393.3906

HAND-DELIVERED BY COURIER

July 5, 2002

Adam Heyward, Product Manager (34)
Regulatory Management Branch #2
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, Crystal Mall #2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
Applicant: Kimberly-Clark Corporation
EPA File Symbol Number: 9402-
Registration Application for New End-Use Product

Dear Mr. Heyward:

On behalf of Kimberly-Clark Corporation (KCC), I am submitting a registration application, under Section 3 of the Federal Insecticide, Fungicide and Rodenticide Act ("FIFRA") for the new end-use product, Kleenex® Brand Anti-Viral Tissue #2. The product is a virucidal tissue. KCC believes that the product will provide an important public-health benefit especially during "cold" season. This submission and its contents contain confidential business information of KCC.

Please note that in December, 2001, KCC submitted a registration application for Kleenex® Brand Anti-Viral Tissue (EPA File Symbol No. 9402-I). Kleenex® Brand Anti-Viral Tissue #2 contains the same active ingredients as Kleenex® Brand Anti-Viral Tissue but different inert ingredients. Consequently, a separate registration application, including product-specific studies, are being submitted for Kleenex® Brand Anti-Viral Tissue #2. The registration application for Kleenex® Brand Anti-Viral Tissue was voluntarily withdrawn by KCC in January, 2002.

As you may recall, a meeting to discuss the registration requirements for an antiviral tissue product was held on February 6, 2001. KCC's meeting minutes and the Agency's response are presented in Attachment 1.

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In support of the registration application for Kleenex® Brand Anti-Viral Tissue #2, the following administrative documents and studies are being submitted:

Administrative Documents

- Application for Pesticide Form.
- Confidential Statement of Formula (including attachment describing the derivation of active and inert ingredient concentrations).
- Certification with Respect to Citation of Data Form.
- Data Matrix (both generic and product specific matrices are included).
- Proposed Product Label (5 copies).
- Agent Authorization Letter.

Studies (3 copies of each study are being submitted)

- Product Chemistry - the individual studies are listed on the attached data transmittal letter.
- Acute Toxicity - the individual studies are listed on the attached data transmittal letter.
- Efficacy - the individual studies are listed on the attached data transmittal letter. Please note that a summary report from a consumer survey sponsored by KCC (Volume 18) that evaluated time-frames for tissue disposal is also being submitted. The consumer survey report supports the 15-minute contact time that is necessary for product efficacy.
- Summary of acute toxicology studies including comments on the eye irritation study and the waiver request for the acute inhalation study.
- Generic toxicity waiver request.
- Exposure assessment concerning the manufacture and use of Kleenex® Brand Anti-Viral Tissue #2.

Labeling Issues

There are two labeling issues that are critical to this application. First, KCC is requesting that the Agency not require the "Keep Out of Reach of Children" or "KOROC" statement, pursuant to 40 C.F.R. §156.66, on the product label. There are several reasons for not requiring the KOROC statement.

- The active ingredients in Kleenex® Brand Anti-Viral Tissue #2 have been extensively reviewed by the Agency and are considered "minimum risk pesticides" pursuant to FIFRA Section 25(b) and 40 C.F.R. §152.25(g). Consequently, both of these active ingredients can be currently marketed in pesticide products that do not have to be registered under FIFRA and, therefore, do not have to include the KOROC statement in their labeling.

- Citric acid is widely used in numerous foods consumed by children such as beverages, ice-cream, candy, and baked goods and sodium lauryl sulfate is used as a surfactant in shampoos, skin cleansers and bath and shower products. Consequently, child exposure to both citric acid and sodium lauryl sulfate is widespread. A search of toxicological data bases did not reveal any information associating either citric acid or sodium lauryl sulfate with adverse effects in children.

- For several years, KCC has marketed a silicone treated tissue, under the brand name Kleenex® UltraSoft Facial Tissue, that contains similar inert ingredients at similar concentrations as those used in Kleenex® Brand Anti-Viral Tissue #2. There have been no reports from consumers or other public-health related individuals to KCC of any untoward effects in children from the use of the silicone treated tissue. In this regard, it should be noted that KCC maintains a state-of-the-art system for obtaining and evaluating consumer complaints Accordingly, it is highly likely that the KCC system would have captured any consumer incidents.

- The nature of the product - tissue - makes it unlikely that the KOROC statement will have any positive benefit. Either consumers will ignore the statement since the product is a tissue or consumers will avoid the product since a tissue that must be kept away from children will be viewed as hazardous and/or useless.

- Finally, consistent with the revised labeling regulations (40 C.F.R. §156.66), the product meets the criteria of intended use on children, which is one of the authorized basis upon which the KOROC statement can be waived.

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The second critical label issue is the "signal word". KCC is requesting that the Agency not require a signal word for Kleenex® Brand Anti-Viral Tissue #2. As you are aware, the Agency no longer requires a signal word for Category IV products (40 C.F.R §156.64). The acute oral, dermal, and primary skin irritation studies conducted with Kleenex® Brand Anti-Viral Tissue #2 were all Category IV and the product is not a dermal sensitizer. Although mild irritation was observed in the eye irritation study, the study director noted that the irritation was likely an artifact of the test system rather than a real effect due to the test substance. Accordingly, the study director has provided KCC with an opinion that the eye irritation study should probably be classified as Category IV. A copy of study director's comments is included in the summary document for the acute toxicology studies. Additionally, this effect is noted in the conclusion to the study report.

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark
Corporation

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LEWIS &
HARRISON
Consultants in Government Affairs

122 C Street, N.W., Suite 740
Washington, D.C. 20001
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July 5, 2002

Adam Heyward, Product Manager (34)
Regulatory Management Branch #2
Antimicrobial Division (7510C)
Office of Pesticide Programs
Environmental Protection Agency
1921 Jefferson Davis Highway, Crystal Mall #2
Arlington, VA 22202

re: **Product: Kleenex® Brand Anti-Viral Tissue #2**
Applicant: Kimberly-Clark Corporation
EPA File Symbol Number: 9402-
Data Transmittal Letter for Studies Supporting FIFRA Section 3 Registration of a New End-Use Product

Dear Mr. Heyward:

On behalf of Kimberly-Clark Corporation, I am submitting three (3) copies of the following studies:

Product Chemistry

- Volume 1 of 18
  Kleenex® Brand Anti-Viral Tissue #2: Product Identity and Composition, Description of Beginning Materials, Manufacturing Process and Discussion of Impurity Formation
  MRID#

- Volume 2 of 18
  Kleenex® Brand Anti-Viral Tissue #2: Analysis and Certification of Product Ingredients and Analytical Method to Verify Certified Limits
  MRID#

- Volume 3 of 18
  Silicone Coated Tissue: Verification of Active Ingredients, Storage Stability and Weight of Dry Tissue
  MRID#

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- Volume 4 of 18
  Silicone Coated Tissue: Storage Stability and Weight of Dry Tissue
  MRID#

Exposure Study

- Volume 5 of 18
  Kleenex® Brand Anti-Viral Tissue #2: Potential Exposure to the Product's Active Ingredients During Manufacture and Use
  MRID#

Toxicology Studies

- Volume 6 of 18
  Waiver Request for Generic Toxicity Data
  MRID#

- Volume 7 of 18
  Kleenex® Brand Anti-Viral Tissue #2: Summary of Acute Toxicology Studies and Waiver Request for Acute Inhalation Study
  MRID#

- Volume 8 of 18
  Acute Oral Toxicity/LD50 in Rats
  MRID#

- Volume 9 of 18
  Acute Dermal Toxicity/LD50 in Rats
  MRID#

- Volume 10 of 18
  Acute Eye Irritation in Rabbits
  MRID#

Toxicology Studies (cont.)

- Volume 11 of 18
  Acute Dermal Irritation in Rabbits
  MRID#

- Volume 12 of 18
  Delayed Contact Sensitization Test - Buehler Method
  MRID#

Efficacy Studies

- Volume 13 of 18
  Virucidal Efficacy of Facial Tissue - For Treated and Untreated Tissue Against Rhinovirus 1A, ATCC VR-1364
  MRID#

- Volume 14 of 18
  Virucidal Efficacy of Facial Tissue - For Treated and Untreated Tissue Against Rhinovirus 2, ATCC VR-482
  MRID#

- Volume 15 of 18
  Virucidal Efficacy of Facial Tissue - For Treated and Untreated Tissue Against Influenza A, ATCC VR-1469
  MRID#

- Volume 16 of 18
  Virucidal Efficacy of Facial Tissue - For Treated and Untreated Tissue Against Influenza B, CDC ID# 2001701156
  MRID#

- Volume 17 of 18
  Virucidal Efficacy of Facial Tissue - For Treated and Untreated Tissue Against Respiratory Syncytial Virus, ATCC VR-26
  MRID#

- Volume 18 of 18
  Consumer Survey: Facial Life Study, Project FACT (Flu and Cold Tissue)
  MRID#

If you have any questions regarding this submission, please contact me at (202) 393-3903, ext. 14.

Sincerely,

Eliot I. Harrison
Agent for Kimberly-Clark Corporation

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Please read instructions on reverse before completing form. Form Approved, OMB No. 2070-0060, Approval expires 05-31-98

B

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☒ Registration
☐ Amendment
☐ Other

OPP Identifier Number
293870

Application for Pesticide – Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
9402-xx RN	Adam Heyward	☒ None ☐ Restricted
4. Company/Product (Name)	PM#	
Kleenex® Brand Anti-Viral Tissue #2	Team 34	
5. Name and Address of Applicant *(Include ZIP Code)*	6. **Expedited Review**. In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:	
Kimberly-Clark Corporation 2100 Winchester Road Neenah, WI 54957 *PLEASE SEND ALL CORRESPONDENCE TO "CONTACT POINT" LISTED BELOW* ☐ *Check if this is a new address*	EPA Reg. No. _____ Product Name _____	

Section – II

☐ Amendment – Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification – Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application
☒ Other – Explain below

Explanation: Use additional page(s) if necessary. (For Section I and Section II.)
Registration application for new end-use product, which is a virucidal tissue. Refer to the cover letter for details regarding the application.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes*	☐ Yes	☐ Yes	☐ Metal
☒ No	☒ No	☒ No	☒ Plastic
	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt. / No. per container	☐ Glass
***Certification must be submitted**			☒ Paper
			☐ Other (Specify)

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	1-150 tissues per retail container	☒ On Label ☐ On labeling accompanying product

6. Manner in Which Label is Affixed to Product ☒ Lithograph ☐ Paper glued ☐ Stenciled ☒ Other Printed on box, overwrap or bag

Section – IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application)*

Name	Title	Telephone No. (Include Area Code)
Eliot Harrison, Lewis & Harrison 122 C Street, NW – Suite 740, Washington DC 20001	Agent for Kimberly-Clark Corporation	202-393-3903 x14

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature	3. Title	6. Date Application Received (Stamped)
Eliot J. Harrison	Agent for Kimberly-Clark Corporation	532
4. Typed Name Eliot Harrison, Lewis & Harrison	5. Date July 5, 2002	

401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to this address.

GENERIC DATA MATRIX

Date July 5, 2002

EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***

Applicant's/Registrant's Name & Address:
Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957

Product
Kleenex® Brand Anti-Viral Tissue #2

Ingredient(s): **Citric Acid (CASRN 77-92-9, Chemical Code 081801)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
			---	---	Footnote 1
			---	---	Footnote 1
			Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
			Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
			---	---	Footnote 2
			Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
			---	---	Footnote 3
			---	---	Footnote 4
			---	---	Footnote 4
			---	---	Footnote 4
			---	---	Footnote 4
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			---	---	Footnote 6

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Signature

Name and Title: **Eliot Harrison, Lewis & Harrison**
Agent for Kimberly-Clark Corp.

Date July 5, 2002

UNITED STATES EN ONMENTAL PROTECTION AGENCY
M Street, S.W.
WASHINGTON, D.C. 20460

Form Approved OMB No. 2070-0060

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GENERIC DATA MATRIX

Date July 5, 2002	EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***	Page 2 of 2
Applicant's/Registrant's Name & Address: **Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957**	Product **Kleenex® Brand Anti-Viral Tissue #2**	

Ingredient(s): **Citric Acid (CASRN 77-92-9, Chemical Code 081801)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note

FOOTNOTES:

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Signature	Name and Title: **Eliot Harrison**, Lewis & Harrison, **Agent for Kimberly-Clark Corp.**	Date July 5, 2002

401 M Street, S.W.
WASHINGTON, D.C. 20460

GENERIC DATA MATRIX

Date July 5, 2002

EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***

Applicant's/Registrant's Name & Address:
Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957

Product
Kleenex® Brand Anti-Viral Tissue #2

Ingredient(s): **Citric Acid (CASRN 77-92-9, Chemical Code 081801)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
40 CFR § 158.150-158.190	**PRODUCT CHEMISTRY**				
830-1550/61-1	Product Identity and Composition	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
830-1600/61-2	Description of the Materials Used to Produce the Product	**Not Applicable**	---	---	Footnote 1
830.1650/61-2	Description of the Manufacturing Process	**Not Applicable**	---	---	Footnote 1
830.1670/61-3	Discussion of Formation of Impurities	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.1700/62-1	Preliminary Analysis	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.1750/62-2	Certified Limits	**Not Applicable**	---	---	Footnote 2
830.1800/62-3	Enforcement Analytical Method	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.6302-6321	Chemical and Physical Properties	**Not Applicable**	---	---	Footnote 3
40 CFR § 158.490	**ECOLOGICAL EFFECTS**				
850.2100/71-1	Acute Avian Toxicity: Bobwhite Quail / Mallard Duck	**Not Applicable**	---	---	Footnote 4
850.2200/71-2	Subacute Avian Toxicity: Bobwhite Quail / Mallard Duck	**Not Applicable**	---	---	Footnote 4
850.1010/72-2	Acute Toxicity to Freshwater Invertebrates	**Not Applicable**	---	---	Footnote 4
850.1075,850.1025,850.1035/72-3	Acute Toxicity – Estuarine/Marine Organisms	**Not Applicable**	---	---	Footnote 4
40 CFR § 158.340	**TOXICOLOGY**				
870.3100/82-1	Subchronic Oral Toxicity, 90 Day – Rodent/Nonrodent	**Waiver Request**	---	---	Footnote 5
870.3200/82-2	Repeated Dose Dermal Toxicity	**Waiver Request**	---	---	Footnote 5
870.3250/82-3	Subchronic Dermal Toxicity, 90 Days	**Waiver Request**	---	---	Footnote 5
870.3465/82-4	Subchronic Inhalation Toxicity, 90 Days	**Waiver Request**	---	---	Footnote 5
870.6100/82-5	90 Day Neurotoxicity	**Waiver Request**	---	---	Footnote 5
870.4100/83-1	Chronic Feeding	**Waiver Request**	---	---	Footnote 5
870.4200/83-2	Oncogenicity	**Waiver Request**	---	---	Footnote 5
870.3700/83-3	Teratogenicity / Developmental Toxicity	**Waiver Request**	---	---	Footnote 5
870.3800/83-4	Reproduction and Fertility Effects	**Waiver Request**	---	---	Footnote 5
870.5100-870.5915/84-2	Genetic Toxicity	**Waiver Request**	---	---	Footnote 5
870.7485/85-1	Metabolism and Pharmokinetics	**Waiver Request**	---	---	Footnote 5
40 CFR § 158.290	**ENVIRONMENTAL FATE**				
835.2110/161-1	Hydrolysis	**Not Applicable**	---	---	Footnote 6

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Signature

Name and Title: **Eliot Harrison, Lewis & Harrison**
Agent for Kimberly-Clark Corp.

Date
July 5, 2002

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Form Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to this address.

GENERIC DATA MATRIX

Date July 5, 2002	EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***	Page 2 of 2
Applicant's/Registrant's Name & Address: **Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957**	Product **Kleenex® Brand Anti-Viral Tissue #2**	

Ingredient(s): **Citric Acid (CASRN 77-92-9, Chemical Code 081801)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note

FOOTNOTES:

* This study is being concurrently submitted with this Data Matrix; therefore, no MRID number has yet been assigned by the US EPA.

1 Manufacturing process information is not applicable since the citric acid used in Kleenex® Brand Anti-Viral Tissue #2 meets both pharmaceutical grade (USP) and food-grade (FCC) requirements. Additionally, citric acid is considered a "minimum risk pesticide" under 20 CFR Part 152.25(g). Since pesticide products that meet the provisions of 152.25(g) are not required to provide manufacturing process information, there is no basis for requiring such information for products that contain 152.25(g) active ingredients but do not qualify as exempt products under 152.25(g) for reasons unrelated to the manufacturing process. In this situation, Kleenex® Brand Anti-Viral Tissue #2 is not eligible for the 152.25(g) exemption since the product makes public-health related claims and contains inert ingredients that are not listed on List 4.

2 Certified limits are not applicable since citric acid is a part of an integrated manufacturing process to make an end-use product, Kleenex® Brand Anti-Viral Tissue #2. Please note that certified limits for citric acid are provided in the end-use product.

3 Chemical and physical property data on citric acid was provided in the Reregistration Eligibility Documents (RED's) for this active ingredient. In addition, citric acid is not being separately registered as a manufacturing-use product (MUP), but is used, as indicated above, in an integrated manufacturing process.

4 Avian and aquatic studies are not applicable since the use pattern for the end-use product, Kleenex® Brand Anti-Viral Tissue #2, is indoor and there is not potential for avian or aquatic exposure.

5 The rationale for waiving the generic toxicology studies is provided in Study Volume 7.

6 The Agency has previously waived all environmental fate data requirements, including the hydrolysis study, for citric acid.

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Signature	Name and Title: **Eliot Harrison**, Lewis & Harrison Agent for Kimberly-Clark Corp.	Date July 5, 2002

Kimberly-Clark

December 20, 2001

Adam Heyward, Product Manager (34)
Regulatory Management Branch #2
Antimicrobial Division (7510C)
Office of Pesticide Programs.
Environmental Protection Agency
1921 Jefferson Davis Highway #2
Arlington, VA 22202

re: Agent Authorization
Company: Kimberly-Clark Corporation
Product: Kleenex Ant-Viral

Dear Mr. Heyward:

This letter authorizes Eliot Harrison of Lewis & Harrison, 122 C St., N.W., Suite #740, Washington, DC, 20001 to act as Kimberly-Clark's agent regarding the FIFRA Section 3 registration application for Kleenex Anti-Viral.

If you have any questions regarding this authorization, please contact me at (920) 721-6835.

Kent E. Willetts

Kent E. Willetts
Kimberly-Clark Corporation
2300 Winchester Road
P.O. Box 2007
Neenah, WI 54957-2007

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Form Approved OMB No. 2070-00

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name: Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957	EPA Registration Number/ File Symbol 9402-XX
Active Ingredient(s) and/or representative test compound(s): Citric acid, Sodium lauryl sulfate	Date July 5, 2002
General use pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor, Non-Food	Product Name Kleenex® Brand Anti-Viral Tissue #2

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).	☒ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data Call-In Notice is supported by all data submitted or cited in the application for registration, the form for reregistration, or this Data Call-In response. In addition, if cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of ... that would be required to be submitted under the data requirements in effect on the date of approval of this application if the ...ication sought the initial registration of a product of identical or similar composition and uses.

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original submitter or that I have obtained the written permission of the original submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the written permission of the original data submitter to use this study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate and complete. I acknowledge that any knowingly false or misleading statements may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
Eliot Harrison	July 5, 2002	Eliot Harrison, Agent for Kimberly-Clark Corp.

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M Street, S.W.
WASHINGTON, D.C. 20460

GENERIC DATA MATRIX

Date **July 5, 2002**

EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***

Applicant's/Registrant's Name & Address:
Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957

Product
Kleenex Brand Anti-Viral Tissue #2

Ingredient(s): **Sodium Lauryl Sulfate (CASRN 151-21-3, Chemical Code 079011)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
40 CFR § 158.150-158.190	**PRODUCT CHEMISTRY**				
830-1550/61-1	Product Identity and Composition	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
830-1600/61-2	Description of the Materials Used to Produce the Product	**Not Applicable**	---	---	Footnote 1
830.1650/61-2	Description of the Manufacturing Process	**Not Applicable**	---	---	Footnote 1
830.1670/61-3	Discussion of Formation of Impurities	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.1700/62-1	Preliminary Analysis	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.1750/62-2	Certified Limits	**Not Applicable**	---	---	Footnote 2
830.1800/62-3	Enforcement Analytical Method	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.6302-6321	Chemical and Physical Properties	**Not Applicable**	---	---	Footnote 3
40 CFR § 158.490	**ECOLOGICAL EFFECTS**				
850.2100/71-1	Acute Avian Toxicity: Bobwhite Quail / Mallard Duck	**Not Applicable**	---	---	Footnote 4
850.2200/71-2	Subacute Avian Toxicity: Bobwhite Quail / Mallard Duck	**Not Applicable**	---	---	Footnote 4
850.1010/72-2	Acute Toxicity to Freshwater Invertebrates	**Not Applicable**	---	---	Footnote 4
850.1075,850.1025,850.1035/72-3	Acute Toxicity – Estuarine/Marine Organisms	**Not Applicable**	---	---	Footnote 4
40 CFR § 158.340	**TOXICOLOGY**				
870.3100/82-1	Subchronic Oral Toxicity, 90 Day – Rodent/Nonrodent	**Waiver Request**	---	---	Footnote 5
870.3200/82-2	Repeated Dose Dermal Toxicity	**Waiver Request**	---	---	Footnote 5
870.3250/82-3	Subchronic Dermal Toxicity, 90 Days	**Waiver Request**	---	---	Footnote 5
870.3465/82-4	Subchronic Inhalation Toxicity, 90 Days	**Waiver Request**	---	---	Footnote 5
870.6100/82-5	90 Day Neurotoxicity	**Waiver Request**	---	---	Footnote 5
870.4100/83-1	Chronic Feeding	**Waiver Request**	---	---	Footnote 5
870.4200/83-2	Oncogenicity	**Waiver Request**	---	---	Footnote 5
870.3700/83-3	Teratogenicity / Developmental Toxicity	**Waiver Request**	---	---	Footnote 5
870.3800/83-4	Reproduction and Fertility Effects	**Waiver Request**	---	---	Footnote 5
870.5100-870.5915/84-2	Genetic Toxicity	**Waiver Request**	---	---	Footnote 5
870.7485/85-1	Metabolism and Pharmokinetics	**Waiver Request**	---	---	Footnote 5
40 CFR § 158.290	**ENVIRONMENTAL FATE**				
835.2110/161-1	Hydrolysis	**Not Applicable**	---	---	Footnote 6

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Signature

Name and Title: **Eliot Harrison**, Lewis & Harrison
Agent for Kimberly-Clark Corp.

Date **July 5, 2002**

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
M Street, S.W.
WASHINGTON, D.C. 20460

Form Approved OMB No. 2070-0060

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GENERIC DATA MATRIX

Date July 5, 2002	EPA Reg. No./File Symbol 9402 - ___ *(not yet assigned)*	Page 2 of 2
Applicant's/Registrant's Name & Address: **Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957**	Product **Kleenex Brand Anti-Viral Tissue #2**	

Ingredient(s): **Sodium Lauryl Sulfate (CASRN 151-21-3, Chemical Code 079011)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note

FOOTNOTES:

* This study is being concurrently submitted with this Data Matrix; therefore, no MRID number has yet been assigned by the US EPA.

1 Manufacturing process information is not applicable since sodium lauryl sulfate is considered a "minimum risk pesticide" under 20 CFR Part 152.25(g). Since pesticide products that meet the provisions of 152.25(g) are not required to provide manufacturing process information, there is no basis for requiring such information for products that contain 152.25(g) active ingredients but do not qualify as exempt products under 152.25(g) for reasons unrelated to the manufacturing process. In this situation, Kleenex® Brand Anti-Viral Tissue #2 is not eligible for the 152.25(g) exemption since the product makes public-health related claims and contains inert ingredients that are not listed on List 4.

2 Certified limits are not applicable since sodium lauryl sulfate is a part of an integrated manufacturing process to make an end-use product, Kleenex® Brand Anti-Viral Tissue #2. Please note that certified limits for sodium lauryl sulfate are provided in the end-use product.

3 Chemical and physical property data on sodium lauryl sulfate was provided in the Reregistration Eligibility Documents (RED's) for this active ingredient. In addition, sodium lauryl sulfate is not being separately registered as a manufacturing-use product (MUP), but is used, as indicated above, in an integrated manufacturing process.

4 Avian and aquatic studies are not applicable since the use pattern for the end-use product, Kleenex® Brand Anti-Viral Tissue #2, is indoor and there is not potential for avian or aquatic exposure.

5 The rationale for waiving the generic toxicology studies is provided in Study Volume 7.

6 The Agency has previously waived all environmental fate data requirements, including the hydrolysis study, for sodium lauryl sulfate.

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Signature	Name and Title:	Date
	Eliot Harrison, Lewis & Harrison Agent for Kimberly-Clark Corp.	July 5, 2002

WASHINGTON, D.C. 20460

GENERIC DATA MATRIX

Date July 5, 2002

EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***

Applicant's/Registrant's Name & Address:
Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957

Product
Kleenex Brand Anti-Viral Tissue #2

Ingredient(s): **Sodium Lauryl Sulfate (CASRN 151-21-3, Chemical Code 079011)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
			---	---	Footnote 1
			---	---	Footnote 1
			Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
			Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
			---	---	Footnote 2
			Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
			---	---	Footnote 3
			---	---	Footnote 4
			---	---	Footnote 4
			---	---	Footnote 4
			---	---	Footnote 4
			---	---	Footnote 5
			---	---	Footnote 5
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			---	---	Footnote 5
			---	---	Footnote 5
			---	---	Footnote 5
			---	---	Footnote 5
			---	---	Footnote 5
			---	---	Footnote 6

238

Signature

Name and Title: **Elliot Harrison**, Lewis & Harrison
Agent for Kimberly-Clark Corp.

Date July 5, 2002

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Form Approved OMB No. 2070-0060

GENERIC DATA MATRIX

Date July 5, 2002	EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***	Page 2 of 2
Applicant's/Registrant's Name & Address: **Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957**	Product **Kleenex Brand Anti-Viral Tissue #2**	

Ingredient(s): **Sodium Lauryl Sulfate (CASRN 151-21-3, Chemical Code 079011)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note

FOOTNOTES:

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Signature	Name and Title:	Date
	Eliot Harrison, Lewis & Harrison **Agent for Kimberly-Clark Corp.**	July 5, 2002

END USE DATA MATRIX

Date July 5, 2002

EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***

Applicant's/Registrant's Name & Address:
Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957

Product
Kleenex® Brand Anti-Viral Tissue #2

Ingredient(s): **A) Citric Acid (CASRN 77-92-9, Chemical Code 021801)**
B) Sodium Lauryl Sulfate (CASRN 151-21-3, Chemical Code 079011)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
40 CFR § 158.150-158.190	**PRODUCT CHEMISTRY**				
830.1550/61-1	Product Identity and Composition	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
830.1600/61-2	Description of the Materials Used to Produce the Product	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
830.1650/61-2	Description of the Manufacturing Process	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
830.1670/61-3	Discussion of Formation of Impurities	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
830.1700/62-1	Preliminary Analysis	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
		*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 5
830.1750/62-2	Certified Limits	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.1800/62-3	Enforcement Analytical Method	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.6302/63-2	Color	**Not Applicable**	--	---	Footnote 1
830.6303/63-3	Physical State	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 1
830.6304/63-4	Odor	**Not Applicable**	--	---	Footnote 1
830.7200/63-5	Melting Point	**Not Applicable**	---	---	Footnote 2
830.7220/63-6	Boiling Point	**Not Applicable**	---	---	Footnote 2
830.7300/63-7	Density/Relative Density/Bulk Density	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 2
830.7840/63-8	Solubility (Column elution/shake flask)	**Not Applicable**	---	---	Footnote 2
830.7950/63-9	Vapor Pressure	**Not Applicable**	---	---	Footnote 2
830.7370/63-10	Dissociation Constant	**Not Applicable**	---	---	Footnote 2
830.7550/7560/7570/63-11	Partition Coefficient	**Not Applicable**	---	---	Footnote 2
830.7000/63-12	pH	**Not Applicable**	---	---	Footnote 2
830.6313/63-13	Stability	**Not Applicable**	---	---	Footnote 2
830.6314/63-14	Oxidation/Reduction: Chemical Compatibility	**Not Applicable**	---	---	Footnote 2
830.6315/63-15	Flammability	**Not Applicable**	---	---	Footnote 2
830.6316/63-16	Explodability	**Not Applicable**	---	---	Footnote 2
830.6317/63-17	Storage Stability	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 3
		*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 4
830.7100/63-18	Viscosity	**Not Applicable**	---	---	Footnote 2
830.6319/63-19	Miscibility	**Not Applicable**	---	---	Footnote 2
830.6320/63-20	Corrosion Characteristics	**Not Applicable**	---	---	Footnote 2
830.6321/63-21	Dielectric Breakdown Voltage	**Not Applicable**	---	---	Footnote 2

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Signature

Name and Title: **Eliot Harrison**, Lewis & Harrison
Agent for Kimberly-Clark Corp.

Date July 5, 2002

UNITED STATES EN ONMENTAL PROTECTION AGENCY
...1 M Street, S.W.
WASHINGTON, D.C. 20460

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END USE DATA MATRIX

Date July 5, 2002

EPA Reg. No./File Symbol **9402 - ___ *(not yet assigned)***

Applicant's/Registrant's Name & Address:
Kimberly-Clark Corporation, 2100 Winchester Road, Neenah, WI 54957

Product
Kleenex® Brand Anti-Viral Tissue #2

Ingredient(s): **A) Citric Acid (CASRN 77-92-9, Chemical Code 021801)**
B) Sodium Lauryl Sulfate (CASRN 151-21-3, Chemical Code 079011)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
40 CFR § 158.340	**TOXICOLOGY**				
870.1100/81-1	Acute Oral Toxicity	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 8
870.1200/81-2	Acute Dermal Toxicity	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 9
870.1300/81-3	Acute Inhalation Toxicity	**Waiver Request**	---	---	Study Volume 6 Footnote 3
870.2400/81-4	Primary Eye Irritation	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 10
870.2500/81-5	Primary Dermal Irritation	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 11
870.2600/81-6	Skin Sensitization	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 12
40 CFR § 158.640	**PRODUCT PERFORMANCE**				
	Efficacy against Rhinovirus 1A	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 13
	Efficacy against Rhinovirus 2	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 14
	Efficacy against Influenza A	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 15
	Efficacy against Influenza B	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 16
	Efficacy against Respiratory Syncytial Virus	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 17
	Consumer Survey Study	*	Kimberly-Clark Corp. (#9402)	OWN	Study Volume 18

FOOTNOTES:

* This study is being concurrently submitted with this Data Matrix; therefore, no MRID number has yet been assigned by the US EPA.

1 As per PR Notice 92-5, color and odor are not required for end-use products.

2 The end-use product, Kleenex® Brand Anti-Viral Tissue #2, is a tissue and there is no expressable liquid from this tissue. Therefore, these study requirements are not applicable.

3 Kimberly-Clark is requesting that the Agency waive the acute inhalation study for Kleenex® Brand Anti-viral Tissue #2 since inhalation exposure will not occur under conditions of use. The product is a tissue into which is a virucidal component has been impregnated. Unlike disinfectant wipe products, the tissue does not contain any solution that can be expressed during normal use. Accordingly, inhalation exposure is extremely unlikely.

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Signature	Name and Title:	Date
Eliot Harrison	**Eliot Harrison**, Lewis & Harrison **Agent for Kimberly-Clark Corp.**	July 5, 2002

EPA Reg #9402-10

Page ____ is not included in this copy.

Pages 242 through 244 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

✓ The document is a duplicate of page(s) 143-145.

____ The document is not responsive to the request.

The information not included is generally considered confidenti by product registrants. If you have any questions, please conta the individual who prepared the response to your request.

EPA Req #9402-10

Page____ is not included in this copy.

Pages 245 through 246 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

__✓__ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

FOR OFFICIAL USE ONLY

FILE SYMBOL
9402-RN
REGISTRATION NO.

CONFIDENTIAL STATEMENT OF FORMULA ENCLOSED

DATE SUBMITTED	SUBMITTED BY (✓)	
	APPLICANT	BASIC SUPPLIER
7/9/02		

Do Not Write Comments, Formula, or Parts of Formula on This Envelope

NOTE

It shall be unlawful—for any person to use for his own advantage or to reveal, other than to the Secretary, or officials or employees of the United States Department of Agriculture or other Federal agencies, or to the courts in response to a subpoena, or to physicians, and in emergencies to pharmacists and other qualified persons, for use in the preparation of antidotes, in accordance with such directions as the Secretary may prescribe, any information relative to formulas of products acquired by authority of Section 4 of the "Federal Insecticide, Fungicide, and Rodenticide Act."

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Note to reviewer: All text in brackets [xxx] is optional and may or may not be included on a final label.
All text in braces {xxx} is administrative and will not appear on a final label.
Final packaging may be translated into French and/or Spanish

{*FRONT PANEL:*}

{*Primary Brand Name:*} Kleenex® Brand Anti-Viral* Tissue #2

Net Contents: [1 through 150] 3-Ply [White] [Printed] Tissues 8.6x 8.4in / 21.8 x 21.3 cm

ACTIVE INGREDIENTS:
Citric Acid.....7.51%
Sodium Lauryl Sulfate.....2.02%
INERT INGREDIENTS:.....90.47%
Total:.....100.0%

Kleenex® Brand [Tissue]

Open Here

[Date code]

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Note to reviewer: All text in brackets [xxx] is optional and may or may not be included on a final label.
All text in braces {xxx} is administrative and will not appear on a final label.
Final packaging may be translated into French and/or Spanish

{FRONT OR BACK PANEL MARKETING CLAIMS:}

[New] *{"New" will only appear on the label for the first 6 months of distribution}*

[New] [Try-Me] [NOW] [Anti-Viral* Tissue!] [NOW with] [Anti-Viral* Formula!] [Virus*-Neutralizing Formula] [Neutralizes Cold & Flu Viruses*] [Cold & Flu Germs*] [Viruses*!] [Cold & Flu Virus*] [Virus* Neutralizing Layer!] [Kills] [Neutralizes] [99.9% of] [Cold & Flu Germs*] [Cold & Flu Viruses*] [Viruses*] [See back panel for details] {Still just as} [soft]

[Stop Spreading Cold & Flu Germs*] [Anti-Viral* Ingredients]

[Prepare for [Cold & Flu Viruses*] [Viruses*] [Cold & Flu Germs*]]

[Help Stop the Cold & Flu [Virus*] Cycle]

[Help stop the Cycle of Cold & Flu [Viruses*]]

[Help Stop the Spread of [Cold & Flu Germs**] [Cold & Flu Viruses*] [Viruses*]]

[Introducing a revolution in facial tissues!]

[Keep [Cold & Flu] [Viruses*] [Germs*] to Yourself]

[It's Cold & Flu Season – Be Prepared!]

[Now You Can Prepare for Cold & Flu Season]

[Ready for Cold & Flu Season?]

[Help Break the Cycle of] [Cold & Flu Germs*] [Viruses*] [Cold & Flu Viruses*]

[Help Keep [Cold & Flu Viruses*] [Viruses*] [Cold & Flu Germs*] From Spreading]

[KLEENEX® tissue – a barrier of protection against everyday] [cold & flu germs*] [cold & flu viruses*] [viruses*]]

[Block] [Cold [& Flu] Germs*] [Cold [& Flu] Viruses*] [Viruses*]

[New] [KLEENEX® [Ultra Soft] ANTI-VIRAL* Tissues have [GermBlocker*] [Anti-Viral* Blue Layer] [Cold {&Flu] Virus* Lock] [Cold & Flu][Germ Barrier*] [Germ Defense*] [Germ Shield*] a new middle layer [formula] that's [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [viruses*] [germs*] [cold & flu viruses*] [cold & flu germs*] that cause colds and flu. Be prepared with [soft], [three-layered] KLEENEX® ANTI-VIRAL* Tissues.]

[Now KLEENEX® [Ultra Soft] Tissue gives you [a] [an] [super soft] [soft], anti-viral* tissue with a special [moisture activated] middle layer [formula] [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [cold & flu viruses*] [viruses*] [cold & flu germs*.]] [Help Stop the cycle of [cold & flu viruses*] [viruses*] [cold & flu germs*] in your family.] [Try new KLEENEX® [Ultra Soft] ANTI-VIRAL* Tissues today.]

[We're always looking for ways to help keep your family happy. That's why [soft], [new] KLEENEX® [Ultra Soft] ANTI-VIRAL* Tissues have a special middle layer [formula] that's [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [cold & flu germs*] [viruses*] [cold & flu viruses*]. [Buy them for your family this season.]]

[{Scientifically] [Clinically] proven, [New] Kleenex® [Ultra Soft] Anti-Viral* Tissues [neutralize] [kill] [99.9% of] [cold & flu viruses*] [viruses*] [cold & flu germs*].) [Use [new] [super soft] Kleenex® [Ultra Soft] Anti-Viral* tissues to help stop the cycle of [cold & flu germs*] [cold & flu viruses*] [viruses*] in your home.]

[Only KLEENEX® [Ultra Soft] Tissue gives you a tissue with [three] [super soft] [soft] layers, including a middle layer [formula] [scientifically] [clinically] [proven] [to] [that] [neutralize] [kill] [99.9% of] [viruses*] [cold & flu viruses*] [cold & flu germs*].]

[New] [KLEENEX® [Ultra Soft] Anti-Viral* Tissues have a unique [moisture activated] middle layer [formula] [scientifically] [clinically] proven to [neutralize] [kills] [common] [viruses*] [germs*] that cause colds & flu.]

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Note to reviewer: All text in brackets [xxx] is optional and may or may not be included on a final label.
All text in braces {xxx} is administrative and will not appear on a final label.
Final packaging may be translated into French and/or Spanish

[New] [KLEENEX® [Ultra Soft] Anti-Viral* Tissues have three [soft] layers and a special moisture-activated formula [middle layer] that [is] [clinically] [scientifically] [proven to] helps stop the spread of [cold & flu viruses*] [viruses*] [cold & flu germs*].]

[New] [KLEENEX® [Ultra Soft] Anti-Viral* Tissues help stop the spread of [cold & flu germs*] [cold & flu viruses*] [viruses*]. These new tissues have a unique [moisture activated] special middle layer [formula] that [is] [clinically] [scientifically] [proven to] [neutralizes] [kills] [99.9% of] [common] [viruses*] [germs*] that cause colds and flu.]

[New] [KLEENEX® [Ultra Soft] Anti-Viral* Tissues have a moisture-activated middle layer [formula] that [stops] [neutralizes] [kills] most [common] [cold & flu viruses*] [viruses*] [cold & flu germs*].]

[For noses [that just want] extra comfort, now [our] [the] [softest] tissues, Kleenex® [Ultra Soft] Brand Tissues, have Anti-Viral* protection.] [[Scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [cold & flu germs*] [cold & flu viruses*] [viruses*].]

[Our] [the] [softest] [three-layered] Kleenex® [Ultra Soft] Brand Tissues now have Anti-Viral* protection! With a [special] [unique] [moisture activated] middle layer [formula] that is [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [cold & flu germs*] [cold & flu viruses*] [viruses*].]

[Now [our] [the] [softest] [three layered] Kleenex® [Ultra Soft] Brand Tissues gives you an Anti-Viral* middle layer [formula] [scientifically] [clinically] proven to [neutralize] [kill] [99.9% of] [viruses*] [cold & flu viruses*] [cold & flu germs*]. Help stop the cycle of [cold & flu viruses*] [viruses*] [cold & flu germs*] in your family. Try [new] KLEENEX® [Ultra Soft] ANTI-VIRAL* Tissues today.]

[It seems that once one person in the family gets a cold it's only a matter of time before everyone else gets it.] [Introducing new KLEENEX® Anti-Viral [revolutionary] tissues [with a treated middle layer] that kills 99.9% of cold and flu germs [in the tissue].]

[Especially designed for the whole family] [Great for use in hospitals, schools, churches, day care facilities, physicians' offices'.]

[Look for the blue dot pattern.]

[KLEENEX® Anti-Viral tissues with the blue dots.]

[*Thank Goodness for Kleenex® tissue.*],

{Alternate Brand Names:} Kleenex® [Ultra Soft] Brand [with] [Advanced Care] [Anti-Germ*] [Anti-Viral*] [GermBlock*] Tissue

{When final graphics are selected, the name of the graphic will appear above the UPC symbol. The name, while short, typically describes some element of the graphic so that consumers have a specific reference when contacting Kimberly-Clark via the Consumer Services Department.}

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{*BACK PANEL:*}

Directions for Use: It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Use to help prevent the spread of [viruses*] [cold & flu viruses*] [cold & flu germs*]. [Complete] [Total] [99.9%][neutralization] [kill] [inactivation] of [target] viruses* within 15 minutes [after contact].

*Virucidal Against: Rhinoviruses Type 1A and 2 [Rhinoviruses are the leading cause of the common cold], Influenza A and Influenza B [cause of the flu], Respiratory Syncytial Virus [RSV – the leading cause of lower respiratory infection in children].

Storage and Disposal: Store in a dry area. Dispose of used tissues in a normal fashion. Do not reuse empty container.

1-800-553-3639 weekdays 8 a.m. to 4 p.m. CT
Kimberly-Clark Corporation, Dept. [XXX]-108
PO Box 2020, Neenah, WI 54957-2020

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Made in USA {graphic}

www.kleenex.com

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____ Description of quality control procedures.

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____ A draft product label.

✓ The product confidential statement of formula.

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